

SIXTH EDITION

BASIC GYNAECOLOGY

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PREFACE

This book was first published in 1975. It is thus the longest-standing textbook in Gynaecology published in Egypt. Basic Gynaecology has moved into its sixth edition, but the mission has remained the same – to provide basic and current information on a broad range of topics for students, residents, and practising physicians.

All the chapters have been revised and updated. However, with the passage of even a few years, new knowledge will supersede. As usual, I have learned a great deal from preparing this edition, and still teaching others continues to be a great joy to me.

I would like to express my gratitude to Professor Abdel Karim El-Hemaly and Professor Ibrahim Mahrous for providing me with their new concepts in the aetiology, ultrasonographic findings, and surgical treatment of genuine stress incontinence. I am indebted to the publisher Mr. Sayed Mahmoud for his untiring and effective help. I must acknowledge Doctor Essam Hoballah for his invaluable assistance in typing the manuscript. I also thank Mr. Sayed Abd El-Naby for preparing the illustrations.

Farouk Haseeb

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3. Labia Minora (nymphae)

Two thin flaps of nonkeratinized pigmented skin lying within the labia majora on either side of the vaginal orifice. Anteriorly, each labium minor divides into 2 flaps, the upper flaps unite above the clitoris to form the prepuce, while the lower flaps join to form the frenulum of the clitoris. The labia minora unite posteriorly to form a sharp fold of skin called the fourchette. The depression between the fourchette and the hymen is the fossa navicularis. The labium minor contains loose connective tissue devoid of fat and is very vascular so it becomes turgid during sexual excitement. The skin contains many sebaceous glands but no sweat glands or hair follicles.

4. Clitoris

It is the homologue of the penis, lies in front of the symphysis pubis and attached to it by a suspensory ligament. It is 1-2 cm in length and made of glans, prepuce, body and two crura attached to the pubic arches. It consists of erectile tissue and is the most sensitive part of the vulva as it is richly supplied with nerves.

5. Vestibule

It is a triangular area lying within the labia minora with the clitoris at its apex. The external urethral meatus, the vaginal orifice and Bartholin glands open at the floor of the vestibule.

6. The External Urethral Meatus

Present in the anterior part of the vestibule. The Skene tubules are two paraurethral ducts which open in the floor of the urethra 1 cm from the external meatus (4-6 mm in diameter). The Skene tubules are homologous to the prostate in the male. The length of female urethra in the adult is 3-4 cm. Its proximal two-thirds are lined by transitional epithelium and distal third is lined by stratified squamous epithelium.

7. Hymen

A fold of mucous membrane at the vaginal orifice. It consists of fibrous tissue and is covered on both sides by stratified squamous epithelium. It has one or more openings to allow escape of menstrual blood. It may be annular, crescentic, biperforate, cribriform or imperforate. The hymen is torn as a result of sexual intercourse unless it is abnormally elastic. The bleeding is usually slight as the hymen contains few blood vessels. During delivery the hymen becomes destroyed leaving small tags or nodules of fibrous tissue around the vaginal orifice called carunculac myrtiformes or hymenalis.

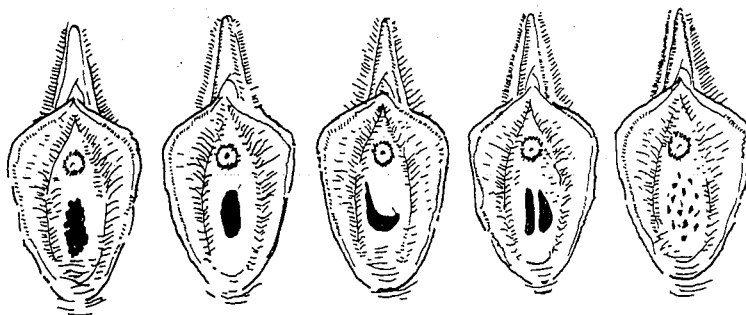


Fig.2. The different shapes of the hymen

8. Vestibular Bulbs

These are two collections of erectile tissue surrounding the vaginal orifice deep to the bulbocavernosus muscles (vaginal sphincter).

9. Bartholin Glands

Two in number. The gland lies embedded in the posterior part of the vestibular bulb, one on either side. The gland is oval and the size of a pea (1 cm in diameter), it has a duct one inch in length which passes medially to open in the floor of the vestibule lateral to the hymen at the 5 and 7 o'clock positions. Normally, the gland is not felt unless diseased and the opening of the duct is not seen. It is a compound racemose gland, the acini are lined by a single layer of columnar epithelium and the duct is lined by transitional epithelium. In response to sexual excitement the gland produces a mucoid colourless secretion to act as a lubricant for coitus. The glands are homologous to Cowper glands in the male.

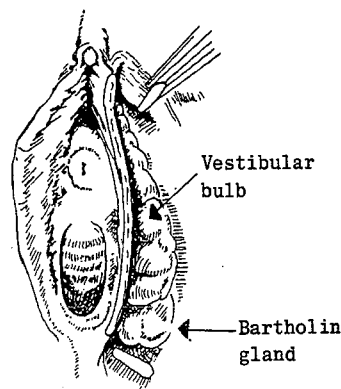


Fig.3. Bartholin gland

BLOOD SUPPLY OF THE VULVA

Branches from the internal and external pudendal arteries. The veins accompany the corresponding arteries, but those from the clitoris join the vaginal and vesical plexuses of veins.

LYMPHATIC DRAINAGE

Inguinal and femoral lymph nodes on both sides because there is crossing of lymphatics. These drain in the lymph node of Cloquet or Rosenmuller present in femoral canal → external iliac glands → common iliac glands → aortic glands.

NERVE SUPPLY

The pudendal nerve supplies motor and sensory fibres to the vulva and perineum. The ilioinguinal, genital branch of genitofemoral and posterior cutaneous nerve of the thigh also give sensory supply to the vulva.

Note for the postgraduate: Distribution of the lymph nodes which drain the vulva:

1. Superficial inguinal nodes. Lateral group which lies below the inguinal ligament, and medial group lying below the external inguinal ring.
2. Deep inguinal nodes. When present the glands lie in the inguinal canal.
3. Superficial femoral nodes. Lateral and medial groups on either side of the great saphenous vein as it enters the femoral vein at the fossa ovalis.
4. Deep femoral nodes. Lie in the femoral canal and usually represented by a single node; the node of Cloquet or Rosenmuller.
5. External iliac nodes. A group medial to the external iliac vein, a group lateral to the external iliac artery, and a third group - if present - in the sulcus between artery and vein.

INTERNAL GENITAL ORGANS

THE VAGINA

Anatomy

It is an elastic fibromuscular tube. It is directed upwards and backwards forming an angle of 60 degrees with the horizon. The upper end is blind and called the vaginal vault. The cervix pierces the upper part of the anterior vaginal wall and divides the vaginal vault into four areas; the anterior fornix in front of the cervix, the posterior fornix which is deep and wide and two lateral fornices. The anterior vaginal wall is about 3 inches in length and the posterior wall is 4 inches in length.

Relations

Anterior wall. It is related to the urinary bladder, urethra, and skene tubules which open into the urethra.

Posterior wall. Its upper third is related to the peritoneum of Douglas pouch, its middle third to the ampulla of the rectum, and its lower third is related to the perineal body.

Lateral wall. Related to the following structures from above downward: cardinal ligament, pelvic connective tissue, levator ani muscle, urogenital diaphragm (triangular ligament) with its attached muscles, vestibular bulb, bulbocavernosus muscle, and Bartholin gland. The ureter lies about 2 cm above the lateral vaginal fornix and 2 cm lateral to the cervix. The uterine artery crosses over the ureter at this point.

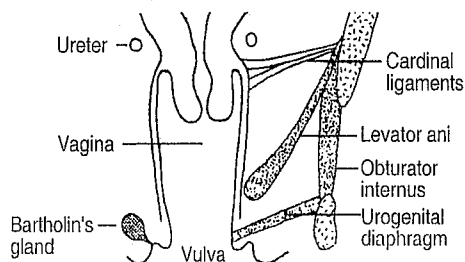


Fig. 3-2. Lateral relations of the vagina.

Structure

1. **Vaginal Mucosa.** It is thrown into transverse folds or rugae which allow the vagina to distend. It is lined by stratified squamous epithelium which contains glycogen. Glycogen is broken down into lactic acid by Döderlein bacilli, so the reaction of the vagina is acidic, the pH is 3.5-4.5 (around 4). The mucosa does not contain glands but the vagina is kept moist by a serous transudate from its wall. Oestrogen stimulates the deposition of glycogen into the vaginal mucosa.
2. **Submucosa.** It is a layer of connective tissue which contains elastic fibres.
3. **Muscle layer.** Made of outer longitudinal and inner circular smooth muscle fibres.
4. Outside the muscle layer there is a sheath of connective tissue.

Blood Supply

Vaginal artery and branches of uterine, internal pudendal, middle and inferior rectal arteries.

Lymphatic Drainage

The upper two-thirds of the vagina drain with the cervix, and the lower third drains with the vulva.

Nerve Supply

Upper two-thirds like the uterus and the lower third receives nerve supply from the pudendal nerve.

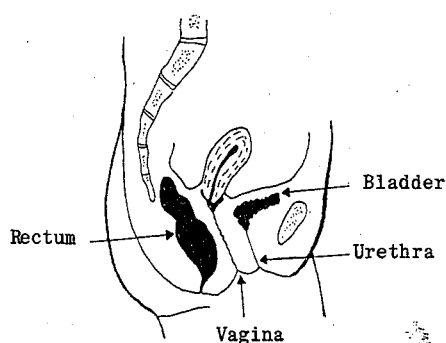


Fig.4. Relations of the vagina

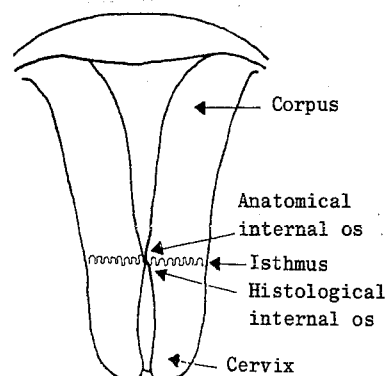


Fig.5. uterus

THE UTERUS

Anatomy

The uterus is a hollow pear-shaped muscular organ. In the nullipara the uterus is 1 inch in thickness, 2 inches across its widest part and 3 inches in length (1 x 2 x 3). In the multipara it is 1.5 x 2.5 x 3.5 inches. The weight is about 40-50 g in the nullipara and 70-80 g in the multipara.

Body

Two or two and half inches in length. The area of insertion of the fallopian tube is called the cornu. The part of the body above the insertion of the fallopian tubes is called the fundus.

Cervix

One inch in length, has a spindle shaped canal which communicates above with the uterine cavity at the anatomical internal os and below with the vagina at the external os. Half of the cervix projects into the vagina (portio vaginalis) and half is above the attachment of the vagina (supravaginal part).

Isthmus

It is a narrow part 1/2-1 cm in length below the anatomical internal os of the cervix. It is the area between the anatomical internal os and histological internal os which is at the junction of uterine mucosa and cervical mucosa (seen microscopically). Progesterone causes contraction and oestrogen causes relaxation of the isthmus. It is lined by modified endometrium with few short glands. During pregnancy the isthmus and lower part of the body of the uterus covered by loose peritoneum form the lower uterine segment.

Relations

The uterus is related anteriorly to the urinary bladder and uterovesical pouch. Posteriorly to Douglas pouch and loops of intestine. Laterally to the contents of the broad ligament including the ureter which lies 2 cm lateral to the cervix (supravaginal part).

Structure of The Body

1. Endometrium or mucous membrane, made of simple tubular glands embedded in a connective tissue stroma. It is lined by columnar ciliated epithelium but the cells lining the glands are non ciliated. The thickness of endometrium varies between 1-8 mm according to the phase of menstrual cycle.
2. Myometrium. Half inch in thickness, its plain muscle fibres are arranged into three layers: outer longitudinal, inner circular and middle interlacing fibres forming figures of 8 around the blood vessels to control bleeding (living ligatures).
3. Peritoneal coat or perimetrium.

Structure of The Cervix

It consists of collagenous connective tissue and smooth muscle fibres (15%). The mucous membrane lining the cervical canal is covered by tall columnar epithelium. Beneath which is a layer of cubical (reserve or basal) cells from which new surface cells develop. The mucosa of cervical canal contains grooves and crypts often referred to as compound racemose glands. The cells lining these crypts secrete mucus. The portio vaginalis is covered by stratified squamous epithelium. The cervical mucus is alkaline (pH 8.5), contains proteins and fructose for nutrition of spermatozoa. It has bactericidal properties to prevent ascent of infection. The

mucous membrane of the endocervical canal of the nullipara is arranged in longitudinal folds, the plicae palmatae, with secondary transverse branching folds, the arbor vitae. These folds disappear following vaginal delivery.

Blood Supply of Uterus

(1) Uterine arteries; (2) branches of ovarian arteries. The uterine artery arises from the anterior branch of the internal iliac artery. The ovarian arteries arise from the aorta.

Lymphatic Drainage. See cervical and endometrial carcinoma.

Nerve Supply

The uterus, cervix, and upper two-thirds of the vagina are supplied by the autonomic nervous system which has both sympathetic and parasympathetic fibres. The sympathetic fibres are derived from the presacral nerve or plexus of nerves which lies in front of the 4th and 5th lumbar vertebrae and sacral promontory. The parasympathetic fibres are derived from the 2nd, 3rd, and 4th sacral nerves. The sympathetic fibres produce muscular relaxation and vasoconstriction, and the parasympathetic fibres produce the opposite effects. The motor sympathetic fibres are derived from T-5, and T-6. Sensory fibres from the body of the uterus accompany the sympathetic nerves which enter the spinal segments T-10, T-11, T-12, and L-1. Sensory fibres from the cervix accompany the 2nd, 3rd, and 4th sacral nerves.

Note. The uterus is sensitive to distension and the cervix is sensitive to dilatation. Both are insensitive to burning, cutting, touch or freezing.

Ligaments Attached to The Body of Uterus

1. The Round Ligaments

Two fibromuscular cords, each is attached to the cornu of uterus and runs laterally via the broad ligament to reach the internal abdominal ring then passes through the inguinal canal to become inserted in the upper part of the labium major in a fanlike fashion. The ligament is supplied by 2 arteries, one branch from ovarian artery (Sampson artery) and one branch from inferior epigastric artery. The round ligaments seem to prevent backward displacement of the uterus. The thickness of the ligament is 5-6 mm, but undergoes marked hypertrophy during pregnancy.

2. Ovarian Ligaments

Two fibromuscular cords, each connects the lower pole of the ovary to the cornu of uterus.

3. Broad Ligaments

Each is a fold of peritoneum running from the side of the uterus to the lateral pelvic wall. Its upper outer part is called the infundibulopelvic ligament which attaches the upper pole of ovary and infundibulum of the tube to the pelvic wall. The broad ligament contains the fallopian tube, the round ligament, the ovarian ligament, the mesovarium, the mesosalpinx,

embryonic remnants of the Wolffian system, the ureter, blood vessels (uterine and ovarian) lymphatics, nerves (sympathetic and parasympathetic) and pelvic connective tissue called parametrium. The ureter passes in the base of the broad ligament.

Cervical Ligaments

These are made of condensed pelvic connective tissue, smooth muscle fibres and elastic tissue. There are 3 pairs of ligaments:

a. The Transverse Cervical Ligaments (*Mackenrodt or Cardinal ligaments*)

Each ligament extends from the lateral side of the supravaginal cervix and vaginal vault and passes laterally in a fan-shaped manner to be inserted in the white line at the lateral pelvic wall. The ureter passes through the ligament in the ureteric canal. The cardinal ligaments form the base of the broad ligaments. The white line is a thickened line in the obturator fascia, which covers the obturator internus muscle.

b. Uterosacral Ligaments

Extend from the supravaginal cervix and vaginal vault and pass backwards surrounding the rectum to be inserted partly in the rectum and partly in the third piece of sacrum.

c. Pubocervical Ligaments

Extend from the supravaginal cervix and vaginal vault and pass forwards beneath the bladder and surrounding the upper part of the urethra to be inserted in the back of the symphysis pubis.

The cervical ligaments are responsible for keeping the uterus at its normal position.

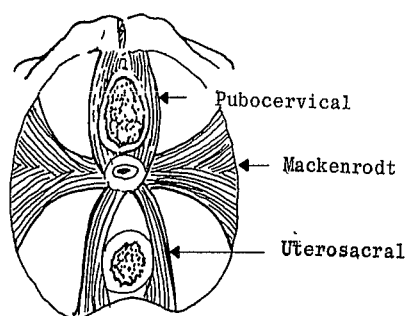


Fig.6. Cervical ligaments

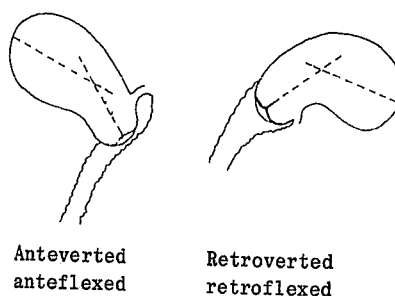


Fig.7. Position of uterus

Position of The Uterus

With the bladder empty, the uterus occupies a central position in the pelvis, with the external os at the level of the ischial spines. Normally, the uterus is anteverted anteflexed. Anteverted means the cervix is bent forwards on the vagina forming an angle of about 90 degrees. Anteflexed means the body of the uterus is bent forwards on the cervix forming an angle of about 160 degrees. In about 15% of normal women, the uterus is retroverted or

retroflexed or both, i.e. retroversion-flexion, or RVF. Retroverted means the cervix is bent backwards on the vagina, so that the external os points downwards and forwards or even directly forwards. Retroflexed means the body is bent backwards on the cervix.

Notes

- Anteversion is caused by development of tone in the uterosacral ligaments and helped by the weight of abdominal organs. Antelexion is due to more growth of the posterior than of the anterior wall of the uterus.
- Cochleate uterus. The cervix is retroverted and the body of uterus is acutely antelexed on the cervix, and so the uterus becomes C-shaped like the cochlea in the ear.

THE FALLOPIAN TUBES

Anatomy

The tube extends from the cornu of the uterus to the ovary. It runs in the upper free border of the broad ligament, about 10 cm in length (8-14 cm). It is divided into 4 parts:

1. The interstitial portion, which runs in the uterine wall, about 1-2 cm in length and 1 mm in diameter.
2. The isthmus, the part immediately lateral to the uterus, 2-3 cm in length and 2 mm in diameter.
3. The ampulla, the widest part about 5 cm in length.
4. Infundibulum or fimbriated end, it has an opening, the abdominal ostium which is surrounded by a number of finger like processes or fimbriae, one of these is longer than the others and is adherent to the ovary (fimbria ovarica).

At the uterotubal junction there is a sphincter to delay the passage of the fertilized ovum to allow for its maturation and to prevent reflux of blood into the peritoneal cavity during menstruation.

Structure

1. Mucous membrane or endosalpinx. It is thrown into longitudinal folds (plicae). It is lined by columnar cells. Some of the cells are ciliated, others are secretory and others are "peg-shaped". These are immature or senile forms of the other types.
2. Muscle layer. Made of outer longitudinal and inner circular smooth muscle fibres.
3. Peritoneal coat. Which is absent along the attachment of the broad ligament.

Blood Supply

Ovarian and uterine arteries. Gangrene of the tube never occurs because of this double blood supply.

Lymphatic Drainage

The same as the ovary.

Nerve Supply

From the ovarian plexus of nerves.

THE OVARY

Anatomy

Oval solid structure, 1.5 cm in thickness, 2.5 cm in width and 3.5 cm in length. Each weighs 4-8 gm. The ovary has an upper pole attached to the pelvic wall by the infundibulopelvic ligament, lower pole suspended to the cornu of the uterus by the ovarian ligament, medial surface, lateral surface, anterior border, attached to the posterior layer of the broad ligament by a fold of peritoneum called the mesovarium and a posterior free border. The ovary lies in a depression on the lateral pelvic wall called "fossa ovarica" which is bounded in front by the obliterated umbilical artery and behind by the ureter and internal iliac artery. The ovary is the only organ in the abdomen which is not covered by peritoneum.

Structure

It is divided into 3 regions. The hilum which gives attachment to the mesovarium and through which pass blood vessels, lymphatics and nerves. The medulla which consists of connective tissue and is surrounded by the cortex. The cortex contains primary follicles in various stages of development. The ovary is covered by the tunica albuginea which is a dense layer of connective tissue. A single layer of cubical epithelium covers the tunica called germinal epithelium which disappears at puberty. At birth each ovary contains about one million primary follicles.

The function of the ovary is production of ova and secretion of hormones, oestrogens, progesterone and androgens (testosterone, androstenedione and dehydroepiandrosterone). It also produces inhibin, activin, and relaxin hormones.

Blood Supply

Ovarian and uterine arteries.

Lymphatic Drainage

- (1) Lymphatics accompany the ovarian blood vessels to reach the aortic lymph nodes;
- (2) obturator, internal, external and common iliac lymph nodes on the same side of the pelvis;
- (3) inguinal lymph nodes by lymphatics which accompany the round ligament.

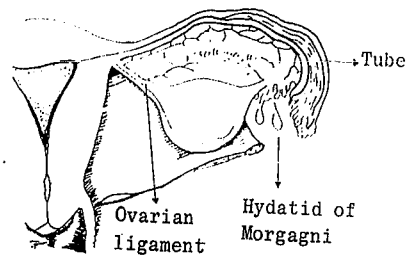


Fig.8. Broad ligament from behind

Nerve Supply

The ovary is supplied by the ovarian plexus of nerves which accompanies the ovarian vessels. The sympathetic nerve fibres arise from ganglia in the celiac and renal areas, and follow the ovarian vessels to reach the ovary and fallopian tube. The sensory fibres reach T-10 and T-11. The parasympathetic fibres are derived from the 2nd, 3rd, and 4th sacral nerves.

The Pelvic Floor

It consists of the following structures from above downwards:

(1) The pelvic peritoneum; (2) extraperitoneal connective tissue; (3) the levator ani muscles which form the pelvic diaphragm; (4) the perineal muscles which include the superficial and deep transverse perineal muscles; the bulbocavernosus, the ischiocavernosus, and the external anal sphincter; (5) subcutaneous fat and fascia; (6) perineal skin.

Notes for the postgraduate

- Superficial transverse perineal muscle. Arises from the ischial tuberosity, and inserts into the perineal body.
- Deep transverse perineal muscle. Arises from the ramus of the ischium, and inserts into the perineal body.
- Bulbocavernosus (bulbospongiosus) muscle. Arises from perineal body and anococcygeal raphe and inserts into the body of the clitoris. It compresses the vestibular bulb, and dorsal vein of the clitoris to maintain its erection (vaginal sphincter).
- Ischiocavernosus muscle. Arises from the ischial tuberosity and ramus of the ischium, and inserts into the undersurface and sides of the crus of the clitoris. It compresses the crus and maintains erection of the clitoris.
- The perineal body. It is a pyramidal elastic fibromuscular mass, rich in elastic tissue, and lies between the anal canal and lower third of the vagina. It receives the insertion of the superficial and deep transverse perineal muscles, the bulbocavernosus muscles, the external anal sphincter muscle, and fibres from levator ani muscles.

The Levator Ani Muscle

It is composed of three parts the pubococcygeus, the iliococcygeus and the ischiococcygeus (coccygeus).

The Pubococcygeus

Arises from the back of the body of the pubic bone and meets its fellow of the opposite side in the middle line. It is pierced by the urethra, vagina and rectum. Some of the fibres are inserted into the urethral, vaginal and rectal walls and are known as pubourethralis, pubovaginalis and puborectalis muscles. The remaining fibres are inserted into the side of coccyx and anococcygeal raphe and known as the pubococcygeus proper. The fibres which decussate between the vagina and rectum are called the fibres of Lushka and they form a strong vaginal sphincter. The fibres decussating between the vagina and urethra are called Bolkagoff fibres.

The Iliococcygeus

Arises from the white line (arcus tendineus) which is a thickening in the obturator fascia and is inserted into the side of the coccyx. The obturator fascia covers the obturator internus muscle.

The Ischiococcygeus

Arises from the ischial spine and is inserted into the side of the coccyx and last piece of sacrum.

Nerve Supply

The perineal branch of 4th sacral nerve which reaches the superior surface of the muscle. and inferior haemorrhoidal nerve (from pudendal nerve) which reaches the inferior surface.

Actions

(1) Support of pelvic organs including the bladder, vagina, uterus, and rectum; (2) sphincteric action for the urethra, vagina and rectum; (3) it is responsible for internal rotation of the head during labour.

Notes

- Injury of levator ani during labour may lead to genital prolapse and stress urinary incontinence.
- The anococcygeal raphe is a midline fibrous band extending from anal canal to the coccyx.

THE PELVIC URETER

Anatomy

The pelvic portion of the ureter is 12-15 cm long. It is about the same length as the abdominal part. Diameter about 3 mm. It enters the pelvis by crossing the end of the common iliac artery and runs downwards into the pelvis anterior to the internal iliac artery and behind the ovarian fossa. When it reaches the ischial spine; it runs forwards and medially towards the bladder passing in the base of the broad ligament in the ureteric canal and below the uterine artery (water "urine" flows under the bridge). In the later part of its course, the ureter lies 2 cm lateral to the cervix (supravaginal part) and 2 cm above the vaginal vault.

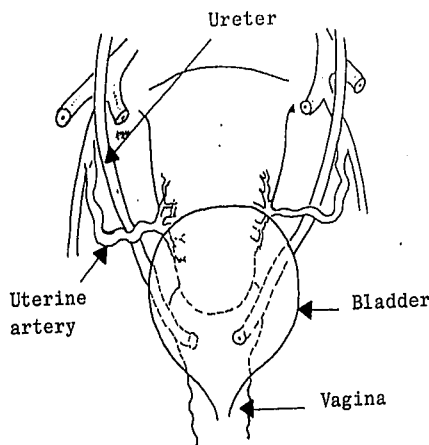


Fig.9. Pelvic ureter

Blood Supply

The pelvic ureter is supplied by a branch from the internal iliac or common iliac artery or lower end of aorta, it also receives branches from the uterine, vaginal, middle rectal and superior vesical arteries.

Dangerous Points of The Ureter

During gynaecological surgery the ureter is liable to be injured at the following sites: (1) at clamping of the infundibulopelvic ligament; (2) at clamping of the uterosacral ligament; (3) when applying the clamp to the uterine artery during hysterectomy; (4) during separation of the bladder from the vagina; (5) during removal of a broad ligament tumour or cervical fibroid which displaces the ureter from its normal site; (6) while closing the peritoneum of the pelvic

floor after hysterectomy; (7) in presacral sympathectomy where the ureters are in relation to the common iliac arteries; (8) in vaginal operations for prolapse.

Methods for Protection of Ureter During Pelvic Surgery

(1) Intravenous pyelography is performed before operation when the ureter is liable to be displaced by the pelvic pathology as in case of a broad ligament tumour or cervical fibroid. This will show the site of the ureter; (2) a ureteric catheter is inserted immediately before operation to allow palpation of the ureter; (3) exposure of the ureter at the pelvic brim and its course is followed downwards; (4) pedicles and ligaments should be clamped under vision and not blindly; (5) subcapsular removal of cervical fibroid as the ureter is outside the capsule.

Ectopic Ureter

The ureter may open in the vestibule which is the commonest abnormal site. Other sites include the urethra, vagina, cervix and uterine body.

Causes of Compression of the Ureter

(1) Pregnancy after the 16th week. The ureters are compressed against the pelvic brim; (2) pelvic tumour especially cervical and broad ligament fibroid; (3) cervical carcinoma infiltrating the parametrium; (4) parametric fibrosis following radiation used for the treatment of malignant lesions as cervical carcinoma; (5) second and third degrees of uterine prolapse.

DEVELOPMENT OF THE FEMALE GENITAL ORGANS

1. The two müllerian (paramesonephric) ducts form the tubes, uterus and the upper two-thirds of the vagina. The lower third of the vagina is developed from the urogenital sinus. This sinus appears as a depression in the caudal end of the embryo and deepens to communicate with the upper part of vagina.
2. The vulva develops from the genital tubercle and genital folds. The genital tubercle appears as a mass of tissue at the caudal end of the abdominal wall and will form the clitoris. Also a longitudinal groove appears on the undersurface of the genital tubercle called urethral groove. This has a urethral fold on each side. The urethral folds will form the labia minora in the female and penile urethra in the male. The urethral groove forms the vestibule. Two genital (labioscrotal) folds appear around the genital tubercle and pass upwards to form the mons veneris and backwards on either side of the urogenital sinus to form the labia majora. The membrane covering the urogenital sinus breaks down and its edges form the hymen. The Bartholin glands and Skene tubules develop as outgrowths of the urogenital sinus.
3. The external genital organs are recognised as female at about 12 weeks of pregnancy, and as male at about 14 weeks when the labio-scrotal folds fuse. If a testis is present it produces testosterone and anti-müllerian hormone (factor). Testosterone is reduced by the 5α -reductase enzyme to form dihydrotestosterone (the active hormone) which will lead to formation of male external and internal genitalia. The antimüllerian hormone inhibits the development of the müllerian duct on the same side by a local action on surrounding tissues and not through the blood stream, i.e. a paracrine effect. So absence of the testis leads to formation of female external and internal genital organs.
4. The ovary develops from the genital ridge which is a thickening in the coelomic epithelium on the medial aspect of the intermediate cell mass of mesoderm. It develops at the level of 10th and 11th dorsal segments and descends into the pelvis by traction of the gubernaculum which is a fibromuscular band extending from the lower pole of the ovary to the inguinal region. The gubernaculum will form the ovarian and round ligaments.
5. The Wolffian duct system consists of 2 longitudinal ducts in which open several transverse tubules. In the male these develop into the epididymis, the vasa efferentia, the vas deferens, and seminal vesicles, but in the female, they atrophy and form embryonic remnants between the two layers of the broad ligaments. These are: (a) Kobelt tubules which are found in the outer part of the broad ligament; (b) epoophoron: few tubules lying between the ovary and the tube; (c) paroophoron: tubules lying between the ovary and the uterus; (d) Gartner or Wolffian (mesonephric) duct which runs between the ovary and the tube then lateral to the body of the uterus, then passes through the lateral wall of the cervix then the antero-lateral wall of the vagina and ends at the clitoris. The embryonic remnants may form a paraovarian cyst between the two layers of the broad ligament or Gartner cyst

into the cervix or vagina. Testosterone stimulates the development of the Wolffian ducts. The ducts degenerate in the female due to lack of testosterone.

Note. Hydatids of Morgagni are pedunculated small cysts found near the fimbriae of the tube. They are remnants of the müllerian ducts.

CONGENITAL ABNORMALITIES OF THE OVARIES

(1) Aplasia or complete absence; (2) ovarian (gonadal) dysgenesis in the form of fibrous bands with no follicles "streak gonads" as seen in Turner syndrome; (3) accessory ovaries; (4) failure of descent into the pelvis; (5) ovotestis which is combined ovarian and testicular tissues seen in the true hermaphrodite.

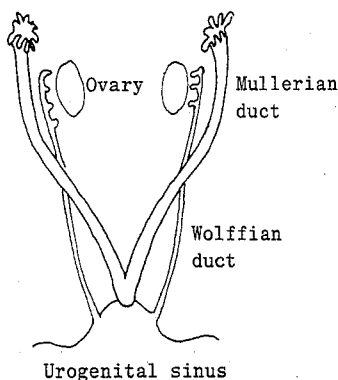


Fig.10. Müllerian and Wolffian systems

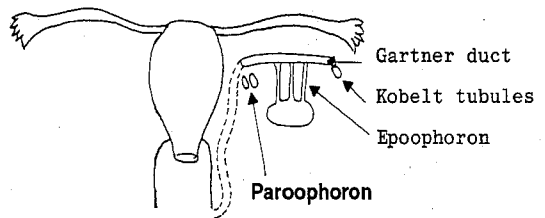


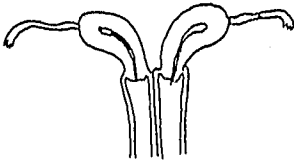
Fig.11. Remnants of the Wolffian system

CONGENITAL ABNORMALITIES OF THE TUBES

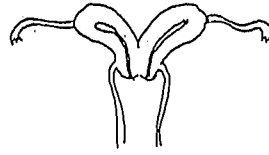
(1) Aplasia; (2) hypoplasia: the tube is long, narrow and tortuous; (3) accessory ostia; (4) congenital diverticulae. These anomalies predispose to tubal pregnancy.

CONGENITAL ABNORMALITIES OF THE UTERUS

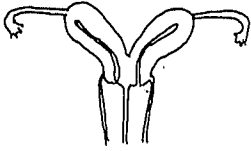
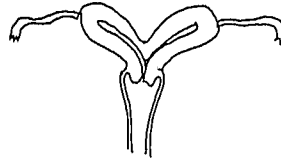
1. **Aplasia, or complete absence.**
2. **Arrest of development:**
 - a. Rudimentary uterus in the form of a solid or hollow muscular nodule.
 - b. Hypoplastic uterus. The total length is less than 6.25 cm (2.5 inches).
 - c. Uterus unicornis. The development of one müllerian duct is completely arrested, so there is only one horn.
 - d. Uterus with a rudimentary horn. One müllerian duct is underdeveloped forming a rudimentary horn which is attached to the uterus by a fibrous band or may communicate with its cavity.
3. **Abnormalities due to incomplete fusion of the müllerian ducts:**
 - a. Uterus didelphys. The 2 müllerian ducts remain separate so that each duct forms a tube, body, cervix, and vagina. The two cervices are at least 2 cm apart.



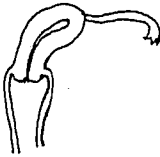
Uterus didelphys



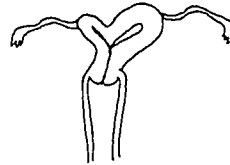
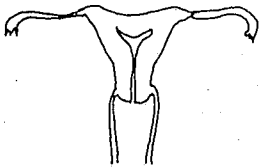
Uterus bicornis bicolis

Uterus bicornis bicolis
with septate vagina

Uterus bicornis unicolis



Uterus unicornis

Uterus with a rudimentary
horn

Arcuate uterus



Subseptate uterus

Fig.12. Congenital uterine abnormalities

- b. Uterus bicornis bicollis. Two uterine bodies and two cervices which are attached together (pseudo-didelphys).
 - c. Uterus bicornis unicollis. Two bodies and one cervix.
 - d. Arcuate uterus (uterus cordiformis); with a depression at the fundus.
 - e. Septate and subseptate uterus.
4. **Congenital elongation of the portio vaginalis of the cervix.** It may be so elongated that the cervix appears from the vagina.

Disorders Associated with Congenital Abnormalities of the Uterus

- 1. Spasmodic dysmenorrhoea occurs with hypoplastic uterus. One sided dysmenorrhoea occurs with bicornuate uterus when one horn is underdeveloped and with uterus unicornis.
- 2. Menorrhagia may occur with a bicornuate uterus due to increased surface area of endometrium.
- 3. Infertility because of uterine hypoplasia or dyspareunia caused by longitudinal vaginal septum.
- 4. Ectopic pregnancy may occur in the rudimentary horn.
- 5. Abortion and preterm labour because of uterine hypoplasia, congenital weakness of uterine isthmus (incompetent cervix) and placentation on a uterine septum which may have poor blood supply (placental insufficiency).
- 6. Malpresentation of the fetus as breech or transverse lie. Habitual malpresentation suggests uterine malformation as bicornuate, septate and subseptate uterus.
- 7. Uterine inertia during labour due to uterine hypoplasia.
- 8. Labour may be obstructed by the nonpregnant horn of a bicornuate uterus or by a longitudinal vaginal septum.
- 9. Placenta accreta when the placenta becomes implanted on uterine septum.

CONGENITAL ABNORMALITIES OF THE VAGINA

- 1. Aplasia. The vagina may be completely absent or is represented by a shallow depression (the part developing from the urogenital sinus).
- 2. Hypoplasia. The vagina is short and narrow.
- 3. Transverse or longitudinal septum.
- 4. Congenital stricture.
- 5. Double vagina (uterus didelphys).
- 6. Congenital ureterovaginal, vesicovaginal or rectovaginal fistula.

Absence of the Vagina

Chromosome analysis is performed to exclude testicular feminization (see amenorrhoea). An ultrasound scan of the renal areas should be undertaken because of the frequent association of renal tract anomalies. Vaginal aplasia is treated by:

1. **Frank Nonoperative Method:** Progressively larger dilators are inserted by the patient or husband to gradually stretch the vagina. Pressure is applied with the dilator for 20 minutes daily. A functional vagina can be created within 6 weeks. This method can be tried before surgery.
2. **McIndoe Operation:** A space is dissected between the urethra and bladder anteriorly and the rectum posteriorly. A plastic mould covered by a split-skin graft (0.5 mm thick) is introduced in the cavity and the labia are sutured over it using silk sutures. The mould is removed after 2 weeks, and the vaginal cavity is irrigated with warm saline solution and inspected. The patient is given a new mould which is used until she starts intercourse, otherwise the vagina will become stenosed (the best dilator is the husband penis). Each night the patient removes the mould, washes it with an antiseptic solution as Betadine before re-insertion.
3. **Williams Operation:** A U-shaped incision is placed over the perineum with the vertical limbs placed over the labia majora. The inner edges are at first sutured together in the midline using chromic catgut; then the outer edges are sutured to make a tube for intercourse.
4. **Thabet Operation:** Like Williams operation, but the transverse limb of the U-shaped incision is placed over the symphysis pubis. Semen will not collect in the created tube.

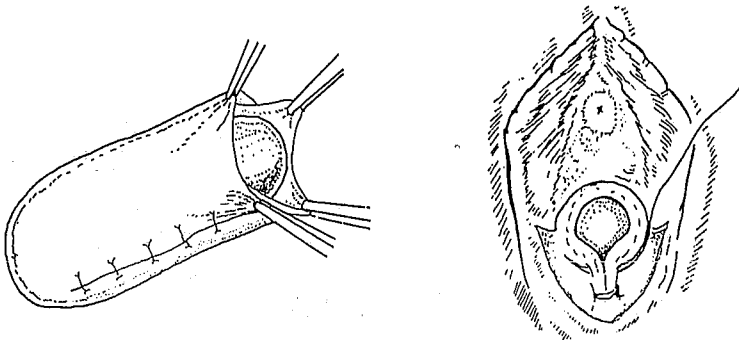


Fig.13. McIndoe operation

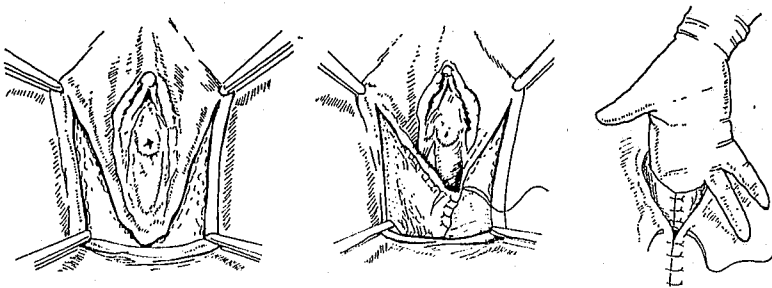


Fig.14. Williams operation

The Mayer-Rokitansky-Kuster-Hauser Syndrome

It is due to failure of development of the müllerian ducts (müllerian agenesis). The vagina is absent or represented by a shallow depression (part developed from urogenital sinus). The uterus is absent or rudimentary. Fallopian tubes are absent or rudimentary. Ovaries are normal because the ovary develops from the genital ridge and not from the müllerian duct. Renal and skeletal abnormalities are frequent (30%, and 15% respectively).

CONGENITAL ABNORMALITIES OF THE VULVA

1. Hypoplasia. Infantile vulva as in Turner syndrome.
2. Cysts as congenital dermoid cyst which occurs only in the midline.
3. Accessory nipple or breast. The breasts and vulva lie in the milk line which extends from the axilla to the vulva.
4. Hypertrophy of the clitoris (clitoromegaly) which is usually associated with other manifestations of virilism.
5. Hypertrophy of one or both labia minora (dog-ear labia minora). This may be congenital or acquired due to frequent masturbation. Also some tribes in Africa attach a weight to the labium minor to make it hanging down as a feature of beauty.
6. Ambiguous external genitalia as in congenital adrenal hyperplasia.
7. Double vulva. There is duplication of the genital tract, urethra, and urinary bladder.

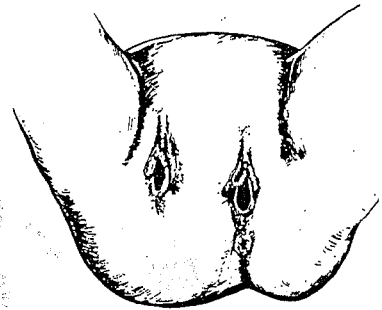


Fig. 14-2. Double vulva.

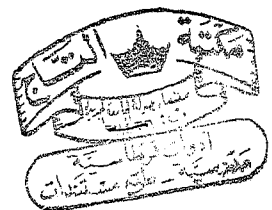
IMPERFORATE HYMEN

Pathology

The menstrual blood accumulates in the vagina every month leading to its distension and formation of a swelling (haematocolpos). In long-standing cases the blood distends the uterus (haematometra) and later the tubes (haematosalpinx). Some of the blood is absorbed and so the retained fluid is dark brown and thick.

Symptoms

- The patient complains of one or more of the following:
1. Primary amenorrhoea.
 2. Lower abdominal pain recurring every month.
 3. An abdominal swelling.
 4. Urinary symptoms as dysuria, acute retention or chronic retention with overflow caused by stretching and compression of the urethra by the distended vagina. The first symptom of imperforate hymen is usually primary amenorrhoea.



Signs

1. In long-standing cases an abdominal mass is felt arising from the pelvis. It is tense cystic and has a limited mobility. The uterus may be felt as a small firm nodule on the top of the mass.
2. Vaginal examination shows a bulging blue closed hymen.
3. Rectal examination shows a tense cystic mass anterior to the rectum and continuous with the abdominal swelling.

Treatment

Under general anaesthesia a cruciate incision is made in the hymen followed by excision of the edges. If it is desired to preserve the hymen, a circular incision is made after applying traction on the centre of the hymen. Antibiotics are given because blood is a good medium for infection and the vaginal resistance is low due to absence of Döderlein bacilli.

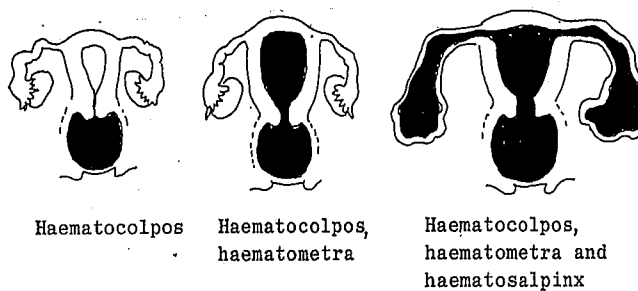
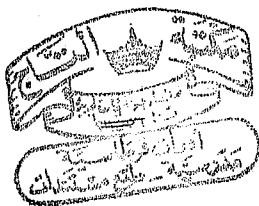


Fig.15. Imperforate Hymen



PHYSIOLOGY OF MENSTRUATION

Menstruation means cyclic uterine bleeding caused by shedding of progestational endometrium. It occurs between menarche (first menstruation) and menopause (physiological cessation of menstruation). Cyclic uterine bleeding caused by shedding of proliferative endometrium is known as pseudomenstruation or anovulatory bleeding.

CHARACTERISTICS OF NORMAL MENSTRUATION

1. Menarche between 10-16 years average 13.
2. Duration of the bleeding 2-7 days (<2 days is hypomenorrhoea and >7 days is menorrhagia).
3. Length of cycle 3-5 weeks, average 4 weeks, estimated from the first day of menstruation to the first day of the next period (<3 weeks is polymenorrhoea and >5 weeks is oligomenorrhoea). Only 15% of women have the typical 28-day cycle.
4. Amount; 30-60 ml, during the whole period. The woman usually uses 3 napkins daily (2 by day and 1 by night). Loss more than 80 ml is abnormal (menorrhagia), and less than 30 ml is hypomenorrhoea.
5. Normally the menstrual blood does not coagulate. At first the blood coagulates in the uterine cavity but is rapidly liquefied by a fibrinolysin enzyme (plasmin) secreted by the endometrium and so the blood becomes devoid of fibrinogen. However, if bleeding is severe or fibrinolysin is deficient, blood clots are passed. In fact, the fibrinolytic system is activated by cell necrosis.
6. The menstrual discharge consists of blood rich in leucocytes, endometrial fragments, cervical mucus, desquamated vaginal epithelial cells, bacteria and enzymes. It also contains prostaglandins, enzymes as alkaline and acid phosphatase.
7. Many women suffer mild symptoms for 7-10 days before menstruation termed "menstrual molimina" which are relieved once menstruation occurs. The symptoms include heaviness in the breasts, irritability or depression. If these symptoms are exaggerated, the condition is called premenstrual syndrome.

THE HYPOTHALAMIC-PITUITARY AXIS

The hypothalamus secretes hormones (factors) which control the activity of the pituitary gland. We have gonadotrophin releasing hormone (GnRH), and prolactin inhibiting hormone which is dopamine. The GnRH stimulates the production of both the follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the basophil cells of the anterior pituitary. Because it secretes more LH than FSH, the GnRH is often called leuteinizing hormone releasing hormone (LHRH). The GnRH is secreted in a pulsatile manner every 60-90 minutes in the follicular phase and every 120-180 minutes in the luteal phase, and reaches the anterior pituitary via the hypophyseal portal vessels.

THE OVARIAN CYCLE

In the first half of the menstrual cycle, the anterior pituitary secretes both FSH and LH. The FSH stimulates the growth of several primary follicles in both ovaries (100-1000). However, only one follicle reaches maturity and forms a graafian follicle which secretes increasing amount of oestrogen (oestradiol). The oestrogen level reaches a peak about 48 hours before ovulation (day 12). This oestrogen peak stimulates increased secretion of LH which reaches a peak about 36 hours before ovulation. The LH peak (surge) leads to ovulation and corpus luteum formation. The LH maintains the growth of the corpus luteum and stimulates it to secrete oestrogen and progesterone. When progesterone reaches a high level it inhibits the secretion of LH. This is followed by degeneration of the corpus luteum. This leads to a drop in the level of oestrogen and progesterone causing separation of the endometrium and menstruation. Also the drop in the level of these hormones stimulates the hypothalamus to secrete more GnRH and thus a new cycle is started in. The life span of the corpus luteum is 14 ± 2 days.

Notes

- Inhibin is a water soluble glycoprotein hormone, secreted by the granulosa cells and inhibits the secretion of FSH and may be involved in the process of follicular atresia. Also secreted by Sertoli cells of the testes.
- Activin is a hormone derived from the ovary and stimulates the secretion of FSH.
- Oestrogen is responsible for the LH surge while progesterone is responsible for FSH surge which also occurs at midcycle.
- Ovulation is due to LH peak. The true mechanism of follicular rupture is unknown.

It may be due to increased intrafollicular pressure, or digestion of collagen fibres in the follicular wall by the proteolytic enzymes. These enzymes are present in the follicular fluid and activated by LH. Also under the influence of LH, prostaglandins increase in the follicular fluid. The prostaglandins may stimulate contraction of smooth muscle fibres in the ovarian stroma leading to follicular rupture.

- When pregnancy occurs, the fertilized ovum secretes human chorionic gonadotrophin (HCG) which stimulates the corpus luteum to grow and form the corpus luteum of pregnancy. This degenerates at 12 weeks when the placenta is formed to carry out its function (secretion of oestrogen and progesterone).
- The mature graafian follicle is 18-24 mm in diameter and consists of (1) ovum; (2) perivitelline space; (3) zona pellucida which is a mucopolysaccharide membrane; (4) corona radiata; (5) cumulus oophorus; (6) cavity filled with liquor folliculi; (7) granulosa cells; (8) theca interna cells; (9) theca externa cells.
- Oestrogen is secreted by the granulosa and theca interna cells of the graafian follicle, the luteinized granulosa cells (lutein cells) and luteinized theca interna cells (paralutein cells) of the corpus luteum, and possibly by stroma cells of the ovary. Progesterone is secreted by the granulosa lutein and theca lutein cells of the corpus luteum.
- The ovary forms oestradiol and oestrone but mainly oestradiol. Oestrone is a metabolite of oestradiol and oestrone and is not formed by the ovary.
- The corpus luteum secretes oestrogen, progesterone, inhibin, and relaxin.

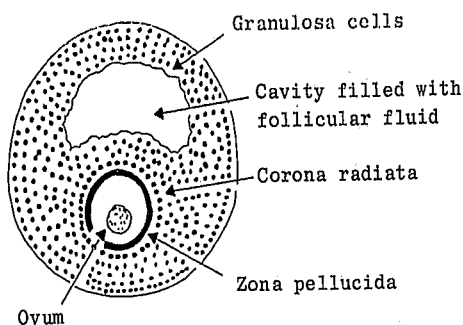


Fig.16. Mature graafian follicle

THE ENDOMETRIAL CYCLE

The changes which occur in the endometrium every month are divided into 3 phases:

1. Menstrual Phase

Two to seven days and during which the superficial functional layer of the endometrium separates leaving the basal layer which contains the basal parts of the glands to allow for regeneration of the endometrium.

2. The Proliferative or Preovulatory Phase

9-10 days, starts after the end of menstruation and ends at the time of ovulation. It is due to the effect of oestrogen produced by the growing graafian follicle and is characterised by:

- a. Thickness of endometrium, 3-4 mm.
- b. Glands are increased in number and length, but remain tubular.
- c. The epithelial cells become low columnar.
- d. Stroma cells increase in size and become globular.
- e. Vascularity is increased.

3. Secretory or Postovulatory Phase

14 $\pm$ 2 days. Its duration is fixed irrespective of the length of the cycle. It begins at ovulation and ends at the onset of menstruation. The endometrium is under the influence of oestrogen and progesterone produced by the corpus luteum and is characterised by:

- a. Thickness of endometrium, 6-8 mm.
- b. Glands continue to grow and become tortuous so that they have a corkscrew or saw-toothed appearance in longitudinal section. The lumen is distended with secretion (glycogen and mucin).
- c. The epithelial cells become high columnar, secretory granules appear at first as subnuclear vacuoles and later as supranuclear vacuoles.
- d. Stroma cells increase in size, become closely packed together and polygonal. The stroma becomes differentiated into three layers:
 - i. Superficial compact layer around the necks of the glands. The stroma cells are closely compacted together.
 - ii. Middle spongy layer around the distended lumens of the glands.
 - iii. Deep compact layer around the basal parts of the glands. The stroma shows oedema, and infiltration with polymorphs and lymphocytes.
- e. Vascularity increases greatly and two types of arterioles can be differentiated:
 - i. Basal arterioles which are short, straight, anastomose freely and supply the basal part of the endometrium.
 - ii. Spiral arterioles which run spirally to supply the superficial layer of the endometrium. They are end arteries and do not anastomose with each other.

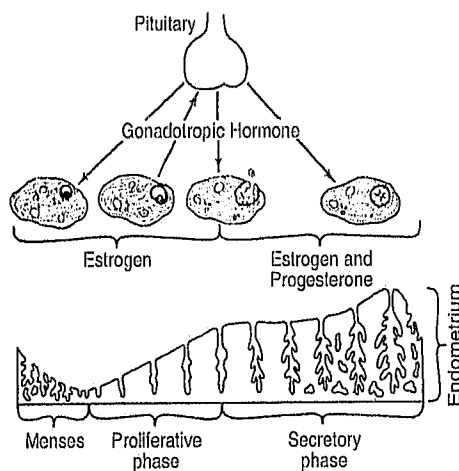


Fig. 17. Ovarian and endometrial cycle.

MECHANISM OF MENSTRUATION

When the corpus luteum degenerates, there is a drop in the level of oestrogen and progesterone leading to reduced oedema and shrinkage of the endometrium causing increasing coiling of the spiral arterioles, ischaemia and necrosis of the superficial and middle layers of the endometrium. The necrotic areas separate leading to bleeding. However, the exact mechanism of menstruation is not yet fully understood. The basal layer of endometrium is not involved because it is supplied by the basal arterioles which anastomose freely. Normally, the endometrium contains prostaglandins (PG) which show a marked increase immediately before and during menstruation. $\text{PGF}_2\alpha$ causes vasoconstriction and myometrial contraction and thromboxane A_2 causes vasoconstriction and aggregation of platelets to form thrombi. In this way the menstrual blood loss is reduced. However, in case of endometrial dysfunction, the endometrium secretes more PGI_2 which is vasodilator and prostacyclin which causes vasodilatation and prevents aggregation of platelets thus resulting in menorrhagia.

CYCLIC CHANGES IN CERVICAL MUCUS

In the follicular phase and under the influence of oestrogen, the cervical mucus becomes excessive, watery, less viscid, clear, acellular, stretchable and shows a positive fern test (see infertility). These changes are maximum at the time of ovulation. In the luteal phase, progesterone makes cervical mucus scanty, thick, viscid, cellular, nonstretchable and gives a negative fern test.

CYCLIC CHANGES IN THE VAGINA

Under the influence of oestrogen, the vaginal smear shows many cells with acidophilic cytoplasm and pyknotic nucleic (small and dark). The back ground is clear with few leucocytes. During the luteal phase, there are many intermediate cells with folded edges (navicular cells), basophilic cytoplasm and vesicular nuclei and are clumped together. The background is misty with many leucocytes.

PUBERTY

It is a physiological phase lasting 2 to 5 years, during which the genital organs mature. The manifestations of puberty in the female include menarche, appearance of secondary sex characters, physical development and psychological changes. Secondary sex characters include development of the breast, appearance of pubic and axillary hair.

The first sign of pubertal development is usually breast growth (thelarche), followed by appearance of pubic hair (pubarche), then axillary hair, then menarche. The mean interval between breast budding and menarche is 2.5 years with a standard deviation of about one year.

Note. Adrenarche means increased activity of the suprarenal cortex at puberty with increased production of adrenal androgens which lead to appearance of pubic and axillary hair.

FEMALE PRECOCIOUS PUBERTY

Definition

It means menarche or appearance of any of the secondary sex characters before the age of 8 years. This applies to North America, as the age of precocious puberty depends upon the population and it is more than 3 standard deviations (3 years) below the mean for the population to which the child belongs.

Types

1. **True (central) precocious puberty.** It is due to increased production of pituitary gonadotrophins.
2. **False (peripheral) precocious puberty.** It is of peripheral origin. It is due to secretion of sex hormones; oestrogen or androgen which is not dependent on pituitary gonadotrophins as in case of oestrogenic or androgenic ovarian tumours. False precocious puberty may be isosexual or heterosexual. A girl who feminizes early is defined as having isosexual precocious puberty. A girl who virilizes early is defined as having heterosexual precocious puberty.
3. **Incomplete precocious puberty.** In this case only one pubertal change as breast development is present before the age of 8 years without the presence of any other pubertal changes and in absence of increased oestrogen production. The other pubertal changes occur at the normal age. Incomplete forms of precocious puberty include premature thelarche (unilateral or bilateral), premature pubarche, and premature adrenarche with appearance of pubic and axillary hair.

Aetiology

1. **Constitutional or idiopathic.** In most cases of precocious puberty (90%) no cause is found. For some unknown reason the hypothalamus stimulates the pituitary gland to secrete its gonadotrophic hormones. There is normal menstruation and ovulation. Pregnancy can occur at young age.

2. **Organic lesions of the brain.** The next common cause. Organic lesions affecting the midbrain, hypothalamus, pineal body, or pituitary gland may lead to premature release of pituitary gonadotrophins. Examples include traumatic brain injury, meningitis, encephalitis, brain abscess, brain tumour as glioma, craniopharyngioma, and hamartomas.
3. **McCune-Albright syndrome.**
4. **Adrenal causes.** (a) Hyperplasia, adenoma, or carcinoma of suprarenal cortex. Congenital adrenal hyperplasia and Cushing syndrome lead to precocious puberty in the male direction, i.e. heterosexual precocious puberty; (b) oestrogen secreting adrenal tumour which is very rare.
5. **Ovarian causes.** (a) Oestrogen producing tumours as granulosa and theca cell tumour; (b) androgen producing tumours as androblastoma; (c) choriocarcinoma because it secretes human chorionic gonadotrophin (HCG) which may stimulate the ovaries to secrete oestrogen; (d) dysgerminoma if it secretes HCG.
6. **Juvenile hypothyroidism.** Lack of thyroxine leads to increased production of thyrotrophin releasing hormone (TRH). The gonadotrophin releasing hormone may also increase leading to increased secretion of pituitary gonadotrophins. In addition to short stature, precocious puberty may occur, also hyperprolactinaemia, and galactorrhoea may occur, as TRH directly stimulates the lactotrophs in the pituitary gland.
7. **Drugs.** Iatrogenic or factitious precocious puberty may follow oral or local administration of oestrogen. A long course of oestrogen cream used for treatment of vulvovaginitis of children may lead to breast development or withdrawal bleeding.
8. **Silver syndrome.** It is a congenital syndrome characterized by a short stature, retarded bone age, and slight or moderate increased gonadotrophin levels which may be associated with precocious puberty.

Diagnosis

1. **History.** It excludes iatrogenic source of oestrogen or androgen. It differentiates between isosexual and heterosexual precocious puberty.
2. **Physical examination.** It diagnoses McCune-Albright syndrome. Neurologic and ophthalmologic examinations exclude organic lesions of the brain.
3. **Special investigations.** These are done according to the history and clinical findings and include:
 - a. Hormonal assay including serum FSH, LH, prolactin, oestradiol, testosterone, 17α -hydroxyprogesterone, TSH, and human chorionic gonadotrophin to diagnose choriocarcinoma.
 - b. Ultrasonography to diagnose ovarian or adrenal tumour.
 - c. Computed tomography or magnetic resonance imaging to diagnose an organic lesion of the brain, or adrenal tumour.

- d. X-ray examination of the hand and wrist to determine bone age. Oestrogen stimulates growth of bone but causes early fusion of the epiphysis. So the child is taller than her peers during childhood, but she is short during adult life. Juvenile hypothyroidism retards bone age, and with Silver syndrome are the only two conditions of precocious puberty in which bone age is retarded and not advanced.

Idiopathic precocious puberty is diagnosed after excluding all other causes.

Treatment

1. Treatment of the cause, e.g., thyroxine for hypothyroidism, removal of ovarian and adrenal tumours.
2. Incomplete forms of precocious puberty do not require treatment, as oestrogen production is not increased.
3. McCune-Albright syndrome is treated with testolactone oral tablets. The drug inhibits the formation of oestrogen from its precursors, so reduces oestrogen level. The dose is 20 mg/kg body weight in 4 divided doses and increased to 40 mg/kg body weight after 3 weeks.
4. Idiopathic type is treated by explanation and reassurance and by giving one of the following drugs which inhibit the secretion of gonadotrophins: (a) gonadotrophin releasing hormone analogues (agonists) which are given as daily nasal spray, intramuscular, or subcutaneous injections every 4 weeks. This is the treatment of choice; (b) medroxyprogesterone acetate tablets (Provera tablets) or intramuscular injection (Depo-Provera); (c) danazol; (d) cyproterone acetate tablets (Androcur). Treatment is given till the age of 12 years (mean age of pubertal development).

McCune-Albright Syndrome

The disease is found more frequently in girls. It consists of a triad of precocious puberty, cystic changes in bones, and café-au lait patches of the skin. The cause of precocious puberty is autonomous production of oestrogen by the ovaries. FSH and LH levels are low. The treatment is testolactone oral tablets which inhibit oestrogen formation by the ovaries.

THE MENOPAUSE AND CLIMACTERIC

The menopause is the permanent cessation of menstruation due to failure of ovarian function. Natural menopause is diagnosed when menstruation has ceased for at least 6 months or 1 year by some gynaecologists in a woman above the age of 40, and in absence of any pathologic cause, so it is a retrograde diagnosis. Menopause is a manifestation of the climacteric which is a transitional phase lasting about 5 years before the menopause and about 5 years after the menopause and during which the ovarian function fails and the genital organs involute.

TYPES OF MENOPAUSE

1. Normal or natural menopause. Occurring between the age of 40 and 55 years with an average of 50 years.
2. Premature menopause. Menstruation ceases before the age of 40. It occurs in about 1% of women below the age of 40.
3. Delayed menopause. Menstruation continues after the age of 55. The causes are: (a) constitutional (a familial or racial tendency); (b) uterine fibroids; (c) diabetes mellitus and; (d) oestrogenic ovarian tumours.
4. Artificial menopause. Caused by surgical removal of both ovaries or their destruction by radium or deep X-ray therapy.

THE MODE OF ONSET OF MENOPAUSE

Menopause may be preceded by (a) hypomenorrhoea; (b) oligomenorrhoea; (c) oligo-hypomenorrhoea; (d) a period of dysfunctional uterine bleeding or (e) menstruation stops suddenly and never recurs. This occurs in about 10% of women.

THE CHANGES ASSOCIATED WITH MENOPAUSE

These are general, local, and hormonal changes.

1. General Changes

- a. Atrophy of the glandular tissue of the breast. However, the breasts may become large and pendulous due to deposition of fat.
- b. Gastrointestinal changes. Appetite may be decreased or increased leading to obesity. There may be various forms of dyspepsia as flatulence and constipation.
- c. Tendency to develop menopausal hypertension. Oestrogen protects against atherosclerosis.
- d. The levels of serum cholesterol and triglycerides rise and the risk of coronary heart disease gradually increases.
- e. Liability to osteoporosis (reduction in the bone mass without a change in the chemical composition of bone). Oestrogen stimulates gut absorption of calcium, reduces calcium loss by kidneys, inhibits the osteoclasts, opposes the action of parathyroid hormone on bone, stimulates calcitonin secretion (calcitonin hormone inhibits the action of

osteoclasts), and facilitates conversion of vitamin D into the active form (1,25-dihydroxy vitamin D).

- f. Mild hirsutism usually occurs. Oestrogen production is decreased leading to decreased synthesis of sex-hormone binding globulin, and so free testosterone is increased.
- g. Psychological changes as headaches, irritability and depression.

2. Local Changes

- a. The pubic hair becomes scanty, grey or white in colour.
- b. Atrophy of the vulva with loss of subcutaneous fat.
- c. The vagina becomes narrow. The mucosa loses its rugae, becomes smooth, thin with little or no glycogen. The vaginal acidity is reduced, the pH becomes neutral or alkaline. This predisposes to infection and senile vaginitis.
- d. The uterus becomes small and atrophic. The portio vaginalis of the cervix may disappear. Senile endometritis may occur.
- e. The ovaries become small, fibrotic and containing no follicles.
- f. The cervical ligaments become atrophic and this may lead to genital prolapse.
- g. Atrophy of the bladder and urethral mucosa. This may lead to frequency of micturition, urgency, stress incontinence and recurrent attacks of cystitis and urethritis.

3. Hormonal Changes

- a. Oestrogen level is low due to absence of ovarian follicles. After menopause the ovary and adrenal glands secrete androgens (mainly androstenedione) which is converted into oestrone. This conversion takes place mainly in body fat but also in the liver, skin and muscles. Because of this peripheral (extraglandular) conversion only 10-50% of women after menopause have oestrogen deficiency. Oestrone is the main oestrogen in postmenopausal women and part of it is converted into oestradiol.
- b. There is increase in the serum levels of follicle stimulating hormone (FSH) and luteinizing hormone (LH). A serum level of FSH above 40 mIU/ml indicates cessation of ovarian function and it precedes the rise in LH level.

Notes for the postgraduate

- 1. Oestradiol comes mainly (90%) from the ovary and a small amount arises by peripheral conversion of testosterone and oestrone.
- 2. Oestrone arises mainly by peripheral conversion of androstenedione and a small amount comes from the ovary.
- 3. Testosterone, and androstenedione come from both the ovaries and adrenal glands.
- 4. Peripheral conversion leads to:
 - Androstenedione → oestrone.
 - Testosterone → oestradiol.
 - Androstenedione ↔ testosterone.
 - Oestrone ↔ oestradiol.
- 5. After menopause, there is a decrease in the production of inhibin and oestradiol by the granulosa cells in the ovary. Decreased inhibin increases FSH. Decreased oestradiol increases FSH and LH to a lesser extent.

6. After menopause androgen production decreases by 50% due to decrease in both ovarian and adrenal production.

MENOPAUSAL SYNDROME

The menopause is associated with mild or no symptoms in about 70% of cases. The symptoms are moderate in 20% and severe in 10%. The symptoms of menopausal syndrome are:

1. **Cardiovascular (vasomotor);** as palpitation, hot flushes, and night sweats. The hot flushes or flashes are present in about 75% of postmenopausal women. They usually disappear after 1-2 years even without treatment as the body adjusts itself to the new low oestrogen level. However, about 25% of cases will continue to have the flushes for more than 5 years. The hot flush is a sensation of heat felt in the chest, neck, face, and head and may spread all over the body. It is due to attacks of subcutaneous vasodilatation and is usually accompanied with tachycardia and excessive sweating. Vasodilatation is followed by vasoconstriction, so after a flush comes a cold shiver. The hot flush lasts for seconds, minutes, and rarely for one hour but usually 3 minutes. Flushes vary in number from one or two in 24 hours to one every 15-30 minutes in a day. The true cause of hot flushes is unknown but most probably due to sudden drop in oestrogen level. However, other sex hormones as androgens and progesterone may be responsible. Progestogens suppress hot flushes but are less effective than oestrogens. Night sweats are the counterpart of hot flushes felt during the daytime (waking time).
2. **Gastrointestinal.** Appetite may be decreased or increased leading to obesity. There may be various forms of dyspepsia as flatulence and constipation.
3. **Psychological;** as headaches, depression, irritability, lack of concentration, poor memory and insomnia. Insomnia is usually the result of night sweats.
4. **Metabolic;** as obesity, osteoporosis, joint pains and backache due to laxity of ligaments and decreased muscular strength.
5. **Sexual.** The libido is unchanged in most cases, but may be increased or decreased. Decreased libido reflects an aging process.
6. **Genitourinary.** The woman may suffer from senile endometritis, senile vaginitis, dryness of the vagina and dyspareunia. Urinary symptoms in the form of frequency, urgency, stress incontinence, and recurrent attacks of cystitis and urethritis.

Note. Oestrogen has nothing to do with libido. It is testosterone which increases the libido.

Treatment

1. General

Explanation and reassurance because menopause is a change in life and not an end of life. Avoid factors which can precipitate hot flushes as hot weather, hot baths, nervousness, excessive intake of coffee or tea, excessive blankets and coverings during sleep.

2. Diet

Control of diet with less fat to avoid obesity. Increase calcium intake and exercise to guard against osteoporosis. If the woman is not receiving oestrogen therapy supply her with extra 1000 mg calcium daily so that the total intake becomes 1500 mg as the normal diet contains 500 mg of calcium. If she is on oestrogen therapy supply her with extra 500 mg calcium.

3. Medical

Symptomatic treatments as sedatives, tranquilizers, stimulants for depression and beta-blockers for tachycardia and palpitation.

4. Hormonal

- a. Oestrogens. Oestrogen is given alone if the uterus has been removed as there is no risk of endometrial hyperplasia and endometrial carcinoma. The indications for oestrogen therapy are:
 1. The presence of menopausal symptoms in the form of (a) hot flushes; (b) senile vaginitis; (c) atrophic vagina causing dyspareunia; (d) urinary symptoms as frequency, stress incontinence, recurrent cystitis and urethritis; (e) psychological disturbances. Treatment is given for at least one year to prevent recurrence of symptoms.
 2. Premature menopause as this predisposes to osteoporosis. Treatment is given at least till the age of 50 years (average age of menopause). This reduces the risk of osteoporosis by 50-60%.
 3. Treatment of osteoporosis.
- b. Combined oestrogen-progestogen therapy. Given if the woman has the uterus as progestogens protect against endometrial hyperplasia, and endometrial carcinoma.
- c. Progestogens alone are given to control hot flushes when oestrogen is contraindicated as in case of acute or chronic liver disease. Progestogens suppress hot flushes but are less effective than oestrogens (medroxyprogesterone acetate tablets, 10-30 mg daily).
- d. Tibolone (Livial). It is a synthetic drug taken orally, one tablet daily. It has oestrogenic, progestogenic, and weak androgenic effects (hormones normally produced by the ovary). The androgenic effects improve libido. About 15% of patients experience irregular uterine bleeding.

5. Nonhormonal Drugs to Control Hot Flushes

Some drugs are tried to control hot flushes if oestrogens are contraindicated. These include the antihypertensive drugs methyl dopa and beta-blockers. Also Agreal capsules (anxiolytic sedative) can be used. They are less effective than oestrogens and have their side effects.

Treatment of Postmenopausal Osteoporosis

In addition to oestrogen, calcium, vitamin D, fluoride, calcitonin and bisphosphonates are used for the treatment of postmenopausal osteoporosis. Calcium slows bone loss but does not increase bone mass. Fluoride is the only known agent which increases bone mass. Bisphosphonates inhibit the osteoclasts and reduce bone resorption. Alendronate (Fosamax) is the most potent bisphosphonate and is given orally. The dose is 5 mg daily for prevention, and 10 mg daily for treatment.

Notes

- Osteopenia means borderline reduction in bone mass. Osteomalacia means increased softness of bone due to reduced mineral content leading to deformities. It is the adult form of rickets.
- The bone formed by sodium fluoride is fragile and more liable to fracture.

PREMATURE MENOPAUSE (PREMATURE OVARIAN FAILURE)

Definition

It means cessation of menstruation (ovarian function) before the age of 40 years due to depletion of ovarian follicles or failure of the primordial follicles to respond to gonadotrophins. It is a condition of hypergonadotrophic-hypogonadism.

Incidence

Premature ovarian failure (POF) affects about 1% of all women under the age of 40.

Aetiology

1. Idiopathic. In most cases no cause is found to explain the increased rate of follicle disappearance.
2. Chromosomal disorders. Some of the mosaic cases of Turner syndrome, pure gonadal dysgenesis, trisomy-18, and trisomy-13.
3. Metabolic disorders. Myotonia dystrophy, 17- α hydroxylase deficiency, and galactosaemia. The galactose metabolites may affect the migration of germ cells to the genital ridge during intrauterine life leading to reduced number of oogonia (ova) in the ovary.
4. Immunological disorders. Di George syndrome and mucocutaneous fungal infections.
5. Autoimmune diseases. As hypothyroidism due to autoimmune thyroiditis, Addison disease, idiopathic thrombocytopenic purpura, and rheumatoid arthritis. These are associated with antiovarian antibodies. Ovarian biopsy shows primordial follicles surrounded by lymphocytes and plasma cells. The exact mechanism of resistance to gonadotrophins is unknown. Autoimmune ovarian failure is known as Blizzard syndrome.
6. Resistant ovary syndrome.
7. Infections. Mumps and pelvic tuberculosis leading to destruction of follicles.
8. Chemotherapy and radiotherapy used for treatment of cancer.

9. Hysterectomy and removal of ovarian cysts may lead to impairment of ovarian blood supply and POF.
10. Smoking leads to premature menopause by 2 years.
11. Undernourishment.
12. Living at high altitudes.

Diagnosis

It is made by the occurrence of amenorrhoea in a woman below the age of 40. The presence of symptoms and signs of oestrogen deficiency as hot flushes. Serum oestradiol is less than 20 picograms/ml and serum FSH is above 40 mIU/ml. If the woman is below the age of 30, chromosomal study should be done to exclude chromosomal anomaly as Turner syndrome. Ovarian biopsy (full-thickness) diagnoses resistant ovary syndrome. The biopsy shows normal number of primordial follicles. In autoimmune disorders the primordial follicles are surrounded by lymphocytes and plasma cells.

Note. Serum FSH between 20 and 40 mIU/ml indicates impending ovarian failure.

Treatment

Oestrogen-progestogen replacement therapy is given to women with POF till the age of 50 years which is the average age of natural menopause to reduce the risk of osteoporosis.

HORMONE REPLACEMENT THERAPY (HRT)

Indications of Oestrogen Replacement Therapy

See before.

Contraindications to Oestrogen Therapy

1. Acute and chronic liver disease.
2. Gallbladder disease. Oestrogen predisposes to cholestatic jaundice and formation of cholesterol stone.
3. Coronary heart disease.
4. Active thrombophlebitis.
5. Recurrent thrombophlebitis and recurrent venous thrombosis.
6. Ophthalmic vascular disease.
7. Existing breast and oestrogen dependent carcinoma.
8. Undiagnosed uterine bleeding.
9. Porphyria.

Diabetes mellitus, and hypertension are not contraindications. Also there is no evidence that oestrogen replacement therapy increases the risk of recurrence after treatment of breast carcinoma.

Advantages of Oestrogen Therapy

1. Relieves menopausal symptoms and improves quality of life.
2. Reduces the risk of osteoporosis by 50-60%.
3. Reduces the incidence of colonic and rectal cancers, but it is not used for prophylaxis.

Complications of Oestrogen Therapy

1. Headache.
2. Breast tenderness and enlargement.
3. Gastric discomfort and nausea.
4. Uterine bleeding.
5. Generalized oedema.
6. Excessive cervical mucus.
7. Increased risk of deep venous thrombosis (2-4 times) and pulmonary embolism (2 times).
This occurs with oral therapy. The risk is present in the first year of use. The risk can be reduced by screening for hereditary deficiency of clotting factors and if present, long-term aspirin is indicated.
8. Gallbladder disease with formation of cholesterol stones and cholestatic jaundice.
9. Slight impairment of glucose tolerance (with oral therapy).
10. Blood pressure may increase (with oral therapy).
11. Endometrial carcinoma. So in the presence of the uterus a progestogen must be given orally for 10-14 days every month (minimal duration for 10 days and optimal duration for 14 days).
12. Slight increase of breast carcinoma if oestrogen is given for more than 10 years. The relative risk is about 1.2. The risk continues for 10 years after cessation of therapy. Progestogens do not oppose the action of oestrogen on breast tissue. In fact oestrogen-progestogen regimen increases the risk of breast cancer beyond that associated with oestrogen alone.

Note. The incidence of endometrial carcinoma will be 4% if the progestogen is given for 7 days, and 2% if given for 10 days, and 0% if given for 14 days.

Regimens of HRT

1. Oestrogen only.
2. Combined oestrogen and progestogen.
3. Progestogen only.
4. Tibolone.

Oestrogen Only

Indicated if the uterus has been removed. In this case a progestogen is not added because there is no risk of endometrial hyperplasia and carcinoma. Also the progestogen may reverse the beneficial effects of oral oestrogens on lipoproteins.

Combined Oestrogen and Progestogen

A progestogen must be added if the uterus is present to prevent endometrial hyperplasia and carcinoma.

Progestogen Only

This is given to control hot flushes when oestrogen is contraindicated as in case of acute and chronic liver disease. Progestogens suppress hot flushes but are less effective than oestrogens.

Medroxyprogesterone acetate (MPA) tablets (Provera tablets) are given as 10-30 mg daily or MPA injection (Depo-Provera) is given 150 mg IM every 3 months.

Tibolone

See treatment of menopausal syndrome.

Oestrogen Only

It is given in the form of oral tablets, skin (transdermal) patch, subcutaneous implant, skin gel, vaginal cream, vaginal tablets, and vaginal ring.

Oral Oestrogens

Conjugated oestrogens (Premarin); the dose is 0.625 mg daily. It is effective in most cases and can be increased to 1.25 mg daily. Another oestrogen is piperazine oestrone sulfate 1 mg daily or oestrinol (Ovestin) 1 mg daily.

Oral therapy is the treatment of choice as it is easy to take, cheaper, and allows good control of the dose.

Transdermal Patch

The patch (Estraderm) is applied twice weekly usually to the buttocks, as the action lasts for 3 to 4 days. It releases oestradiol at a rate of 25, 50, or 100 micrograms per 24 hours. The usual dose is 50 µg/day. It may cause skin reaction in up to 30% of cases. It is more expensive than oral therapy. If the uterus is present, a progestogen is given for 10 days every month, e.g. MPA 10 mg daily for 10 days. Now patches containing oestradiol and a progestogen are available, e.g., Estracombi.

Subcutaneous Implant

Capsules containing 25, 50 and 100 milligrams of oestradiol are available. The 50 mg dose is most commonly used. The capsule is inserted subcutaneously in the abdominal wall using local anaesthesia once every 6 months (4-8 months). In the presence of the uterus a progestogen is given for 10 days each month, or we insert Mirena intrauterine device.

Skin Gel

Gel containing oestradiol is applied to the skin of the arms or legs. The dose is 1-5 mg daily.

Vaginal Cream, Tablet and Ring

For vaginal atrophy and dyspareunia both oral and local oestrogen are given, as oral therapy alone is usually not enough to stimulate growth of vaginal epithelium. Local therapy in the form of vaginal cream (Premarin cream) or vaginal tablet is given for a short course 2-3 months. A vaginal ring (Estring) can be used which releases oestradiol over 3 months.

Oestradiol Nasal Spray

It is used to control hot flushes to avoid the large dose of oestrogen given orally. The dose is 100, 200, 300, or 400 micrograms daily.

Indications of Non-Oral Oestrogen

1. Gastrointestinal problems. Gastric discomfort and the presence of gastritis, ulcer, and malabsorption syndrome.
2. Failure of oral therapy to control symptoms. The parenteral route gives a higher serum oestradiol level.
3. Metabolic disorders. Diabetes mellitus, hypertension, elevated triglycerides and lactose intolerance. Parenteral oestrogen bypasses the liver, so it does not impair glucose tolerance and does not cause hypertension as the liver production of renin substrate and angiotensinogen is not increased. It also lowers the triglycerides. All oral oestrogen and oral progestogen preparations contain lactose as a bulking agent. Hypolactasia (deficiency of lactase activity in the intestine) leads to lactose intolerance and contraindicates oral HRT.
4. History of deep venous thrombosis. Oral oestrogen stimulates the liver to produce clotting factors and inhibits antithrombin III production.
5. Severe osteoporosis. Oestradiol implant gives a high serum oestradiol level with better response.

Combined Oestrogen and Progestogen Therapy

Indicated if the uterus is present.

1. Oestrogen plus cyclic progestogen. A progestogen is given cyclically for 10-14 days every month. An example is to give conjugated oestrogens, 0.625 mg daily and MPA 10 mg daily for 10-14 days. This cyclic progestogen leads to cyclic uterine bleeding (menstruation) in most women. It can also lead to irregular uterine bleeding. Cyclic treatment may be given to perimenopausal women to cause cyclic uterine bleeding.
2. Oestrogen plus continuous progestogen. Conjugated oestrogens, 0.625 mg daily plus MPA 2.5 mg daily. This allows giving a smaller total dose of progestogen to reduce its side effects. This regimen can also lead to irregular uterine bleeding. Continuous treatment is given to women who have been amenorrhoeic for one year.
3. Oestradiol skin patch (Estraderm) plus a progestogen for 10 days every month.
4. Oestradiol-progestogen skin patch, e.g., Estracombi.

5. Progesterone suppositories inserted vaginally or rectally (Cyclogest), or Levonorgestrel intrauterine device (Mirena) can be combined with oestrogen therapy.

Nonhormonal Drugs

Some drugs are tried to control hot flushes if oestrogens are contraindicated. See treatment of menopausal syndrome.

Work up Needed before HRT

1. Detailed history including family history for endometrial and breast cancer.
2. Complete physical examination including the breasts. Blood pressure and weight are recorded.
3. Urine is examined for sugar and protein.
4. Special investigations:
 - a. Fasting blood sugar.
 - b. Serum FSH and oestradiol.
 - c. Lipid profile.
 - d. Endometrial sampling. Done by some gynaecologists in USA.
 - e. Cervical smear.
 - f. Mammogram.
5. Counselling and consent for HRT.

Monitoring of the Patient under Therapy

The patient should be reviewed after:

- Two months: to check side effects, control of symptoms, blood pressure and weight.
- Six months: to ensure that the uterine bleeding is acceptable and to deal with any problem.
- Then every 6 months thereafter: to examine for blood pressure, weight, breasts, and legs.
- Every year, the woman should have a lipogram, mammogram and a cervical smear.

Notes for the postgraduate

1. Conjugated oestrogens are extracted from the urine of pregnant mares. They are a combination of oestrone (50%), equilin, dihydroequilin and other oestrogens.
2. The premenopausal woman needs 1000 mg calcium daily. The postmenopausal woman needs 1500 mg calcium daily. The diet provides 500 mg calcium/d. So after menopause the woman should receive an extra 1000 mg calcium/d if she is not receiving oestrogen therapy and 500 mg/d if she is receiving the therapy.
3. Migraine may or may not be aggravated by HRT, so a trial of treatment is not contraindicated.
4. In menstruating women bone loss occurs at a rate of less than 1% per year. After menopause the rate is 3 to 5% per year.
5. HRT is used by only 38% of women in the United States.

SERMs

SERMs means selective oestrogen receptor modulators. These modulators are nonhormonal compounds different in structure from oestrogens. They stimulate certain – but

not all – oestrogen receptors, hence the name. There are 2 types of oestrogen receptors. Alpha oestrogen receptors present in the breasts and uterus, and beta receptors present in the brain, bone, vagina, urinary bladder, granulosa cells of the ovary, and cardiovascular system. Oestrogen receptors are present in the cell nuclei of target tissues. SERMs include the following:

1. **Tamoxifen (Nolvadex):** It belongs to the first generation of SERMs. It inhibits E receptors in the breasts, but stimulates E receptors in the uterus, bone, and cardiovascular system. It is used in the treatment of breast cancer. However, its use more than 5 years may lead to endometrial hyperplasia, polyposis, carcinoma, sarcomas, adenomyosis, growth of fibroids, and simple ovarian cysts (10%). The latter may be due to direct action causing excessive growth of ovarian follicles.
2. **Clomiphene citrate (Clomid).** It belongs to the first generation of SERMs.
3. **Raloxifene (Evista).** It is the second generation of SERMs. It stimulates oestrogen receptors in bone and vagina, but inhibits oestrogen receptors in the breasts and endometrium. The drug is only used to prevent osteoporosis in postmenopausal women who do not wish to take hormone replacement therapy (HRT) or when it is contraindicated. It does not treat hot flushes, and may increase them. It causes leg cramps in 55% of cases, and slightly increases venous thrombosis. The dose is 60 mg per os daily.
4. **Phyto-oestrogens (Klimadynon).** These are compounds found in certain plants as lentil, peas and soya beans. They have both oestrogenic and antioestrogenic action depending on the target tissue. The oestrogenic effect is weak – about 2% that of oestradiol. These compounds stimulate oestrogen receptors in the brain, and so reduce the number of hot flushes by 50%, also reduce irritability, insomnia, and depression. They also reduce the risk of bone fracture by decreasing osteoclastic activity. They stimulate proliferation of vaginal epithelium, and prevent vaginal dryness, and dyspareunia. They have no effect on breasts or endometrium.

Indications for phyto-oestrogens

1. Women who do not wish to take HRT or when HRT is contraindicated.
2. Women who want to take a natural product for hot flushes.
3. As a supplement to HRT when we do not want to increase the dose of oestrogen.

SECTION II

GYNAECOLOGICAL DIAGNOSIS

HISTORY AND PHYSICAL EXAMINATION

Diagnosis in medicine depends upon the triad of history, physical examination and investigations.

A. HISTORY

1. Personal History

Name, age, marital status, duration of marriage, occupation, nationality, consanguinity, address and telephone number.

2. Complaint

It is taken in the patient own words.

3. Present History

Each complaint is taken in detail. The patient is also asked about urinary symptoms as burning, pain and frequency; and gastrointestinal symptoms as nausea, vomiting, diarrhoea or constipation.

4. Past History

- Past medical history. Ask about the presence of any chronic disease as hypertension, heart disease, diabetes mellitus, renal disease, etc.
- Past surgical history. Ask about any operation done for the patient as appendectomy.
- Hormonal treatment and contraceptive history.
- History of blood transfusion.
- The presence of allergy to drugs, food, etc.
- Exposure to irradiation or radiotherapy.



5. Family History

Ask about conditions that can be inherited as hypertension, heart disease, diabetes mellitus, endocrine disorders, malignant diseases as breast, ovarian, and endometrial carcinoma.

6. Menstrual History

Menarche, duration of menstrual bleeding, length of cycle (D/C), amount (slight, moderate or excessive), the presence of pain and its relation to bleeding, intermenstrual bleeding or discharge. The first day of last menstrual period (LMP).

7. Obstetric History

(a) In each delivery we ask about: (i) duration of pregnancy (preterm, full term, or post-term); (ii) mode of delivery (spontaneous vaginal delivery, by forceps, etc.); (iii) the newborn (male or female, alive or dead); (iv) fetal or maternal complication in the puerperium; (v) time of last delivery. (b) In each abortion, we ask about: (i) duration of pregnancy; (ii) mode of termination (spontaneous or induced); (iii) complication in the postabortive period; (iv) time of last abortion.

8. Sexual History

In case of infertility.

9. Social History

Ask about special habits of medical importance as smoking, alcohol and drugs.

B. PHYSICAL EXAMINATION

I. General Examination

General condition: (good, moderate or bad) and constitution.

Pulse, temperature, blood pressure

Eye examination: Pallor, jaundice, oedema of eye lids

Nose: e.g. saddle nose due to syphilis

Mouth: Tongue, teeth, tonsils

Neck: Thyroid, lymph nodes, congested neck veins

Chest: Heart, lungs, breasts and exclude galactorrhoea

Lower Limbs: Varicose veins, bony deformities, other abnormalities

Note. Six areas of the breast are palpated (four quadrants, area behind the nipple, and axillary tail).

2. Abdominal Examination

The patient should empty her bladder before examination.

- a. **Inspection.** Contour, scar, pubic hair (feminine with an upper straight border, or masculine with a convex upper border), pigmentation as linea nigra, dilated veins, the presence of hernia. To differentiate between an intra-abdominal mass and a mass arising from the anterior abdominal wall, the patient is asked to sit unsupported. If the mass diminishes in size, it is intra-abdominal.
- b. **Palpation.** Superficial to detect tenderness or rigidity, to feel a superficial swelling, arising from the anterior abdominal wall and to gain confidence of the patient and deep palpation to examine the nine areas of the abdomen.
- c. **Percussion.** For any mass present and shifting dullness to detect ascites or internal haemorrhage. A small amount of fluid causes an area of dullness around the umbilicus with the patient in the knee-chest position.
- d. **Auscultation.** If we suspect pregnancy.

3. Pelvic Examination

Vaginal examination includes:

- a. **Inspection.** The various structures of the vulva and perineum are inspected for any abnormality. The patient is asked to cough or strain down to detect prolapse or stress incontinence.
- b. **Digital palpation.** The lubricated index and middle fingers or index finger alone of the gloved right hand are introduced into the vagina until the cervix is reached. The cervix is palpated to detect any abnormality. The anterior, then the posterior vaginal wall is palpated. The urethra is milked from above downwards to detect any discharge. The Bartholin glands are palpated. Normally, the gland is not felt unless diseased and its opening is not seen unless inflamed.
- c. **Bimanual examination.** The two fingers are placed in front of the cervix in the anterior vaginal fornix. The left hand is placed flat on the lower abdomen just above the symphysis pubis. The two hands are pressed together to feel the uterus in between and note any abnormality. If the uterus is retroflexed it cannot be felt through the anterior fornix, but is felt through the posterior fornix. After palpating the uterus, the two fingers are placed in one lateral fornix and the abdominal hand is placed lateral to the uterus to feel the adnexa. Repeat this on the other side. Normally, the tubes are not felt but the ovary may be felt in a thin patient. For every organ or structure palpated in the pelvis – including uterus and cervix – we should report on its site (position), size, shape, surface, consistency, mobility, tenderness, and relation to surrounding structures.
- d. **Speculum examination.** To inspect the cervix and vaginal walls using the Cusco self-retaining vaginal speculum.
- e. **In case of prolapse.** The tone of levator ani muscles is determined by placing two fingers in the vagina and the thumb on the perineum and the patient is asked to cough.
- f. **Rectal examination.** It is performed in certain cases: (i) to examine a virgin; (ii) to diagnose a rectocele or enterocele; (iii) to detect infiltration of uterosacral ligaments in case of cancer of cervix or body. These ligaments are better felt per rectum; (iv) for diagnosis of a mass in Douglas pouch; (v) to examine a rectovaginal fistula and complete perineal tear; (vi) the presence of rectal symptoms as bleeding.

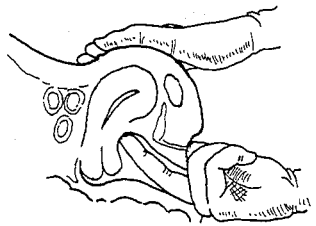


Fig.18. Bimanual examination

Note. The patient should empty the bladder before examination otherwise the uterus will be difficult to define. An exception to the above is when the patient complains of stress incontinence.

C. SPECIAL INVESTIGATIONS

These, vary according to the lesion present. There are noninvasive and invasive methods of investigation.

- a. **Noninvasive investigations.** Cytology, microbiology, hormonal assay, sonography, radiology, computed tomography (CT scan), magnetic resonance imaging, colposcopy and colpomicroscopy.
- b. **Invasive investigations.** Dilatation and curettage, biopsy from suspected lesions, hysterosalpingography, hysteroscopy, laparoscopy and laparotomy.

Note. Culdoscopy has been replaced by laparoscopy.

SONOGRAPHY

INDICATIONS IN GYNAECOLOGY

- A) Diagnostic:** Gynaecologic ultrasound can be used for the diagnosis of: (1) Ovarian cyst or mass; (2) polycystic ovary syndrome; (3) corpus luteum cyst; (4) follicular growth. Ovulation is about to occur when the graafian follicle reaches a diameter of 18-24 mm. This is important in infertile patients to know the response to hormonal treatment and to choose the time of ovum collection for In Vitro Fertilization (IVF); (5) uterine fibroids, endometrial carcinoma, adenomyosis, and intrauterine adhesions; (6) uterine anomalies as bicornuate uterus; (7) missed intrauterine contraceptive device to locate its site; (8) pelvic mass to know its size, site, consistency and nature; (9) breast masses; (10) liver metastases and gallbladder disease; (11) renal abnormalities; (12) ascites; (13) tubal patency by sonohysterosalpingography.
- B) Invasive Procedures:** (1) Retrieval of ova for In Vitro Fertilization; (2) aspiration of simple ovarian cyst, endometriotic ovarian cyst, tubo-ovarian cyst and tubo-ovarian abscess; (3) treatment of intact tubal pregnancy by injecting methotrexate, prostaglandin, potassium chloride or hyperosmolar glucose solution into the intact pregnancy sac; (4) biopsy of recurrent pelvic masses in case of malignancy; (5) placement of intracavitary radium.

The basic principles of sonography and Doppler ultrasound are discussed in "BASIC OBSTETRICS".

SECTION III

MENSTRUAL DISORDERS

DYSMENORRHOEA

Dysmenorrhoea means pain related to menstruation.

TYPES

1. Spasmodic dysmenorrhoea.
2. Membranous dysmenorrhoea.
3. Congestive dysmenorrhoea.

SPASMODIC (PRIMARY, IDIOPATHIC) DYSMENORRHOEA

It is a common complaint in young girls (teenagers). Pain occurs in absence of any organic pelvic lesion.

Clinical Picture

Age

It usually starts 1 or 2 years after menarche because the first cycles are usually anovulatory. This dysmenorrhoea occurs only in ovulatory cycles and usually improves after the age of 25.

Parity

Pain improves or disappears after an abortion or labour because dilatation of the cervix causes laceration of the nerve fibres which transmit pain. Also pregnancy may complete the development of the myometrium and its blood supply.

Family History

There is increased incidence among mothers and sisters of women with primary dysmenorrhoea.

Type of Pain

Pain starts on the first day of menstruation, reaches its maximum within 24 hours while the bleeding is slight, and then improves when the flow becomes established. In few cases pain is felt through the whole period. Pain is colicky, intermittent, felt in the suprapubic region and is often referred to the inner and front sides of the thighs. Pain affects mainly the areas of the body supplied by the first lumbar nerve.

Associated Symptoms

Nausea, vomiting, diarrhoea, and urinary disturbances may accompany pain. These symptoms can be explained by entry of prostaglandin $F_{2\alpha}$ into the systemic circulation. In primary dysmenorrhoea there is increased production of this prostaglandin in the endometrium.

Aetiology

Spasmodic dysmenorrhoea is explained by more than one theory because not all cases arise in the same way.

a. Abnormal Anatomy

1. Cervical obstruction; due to cervical stenosis or retroflexion of the uterus. This causes retention of menstrual blood. The retained blood causes irregular and painful contractions. Also there may be increased reabsorption of prostaglandins from retained blood. At the same time blood may regurgitate along the tubes into the peritoneal cavity leading to peritoneal irritation and pelvic pain.
2. Uterine hypoplasia. The underdeveloped muscle is unable to expel the blood which accumulates causing dysmenorrhoea.

b. Abnormal Physiology

1. Low pain threshold.
2. Ischaemia of uterine muscle, resulting in pain similar to that of angina pectoris.
3. Hypersensitivity of the sympathetic nerve fibres of the uterus. This exaggerates the sensory impulses transmitted along them.
4. Disturbed polarity of the uterus. Uterine polarity means when the fundus contracts the cervix dilates and vice versa dilatation of cervix reflexly causes uterine contraction. The disturbed polarity leads to difficulty in discharge of menstrual blood resulting in pain.
5. Clotting of menstrual blood. The clots are difficult to expel, however, clots may be passed without causing pain.
6. Hormonal imbalance. Relative excess of progesterone causes contraction of the uterine isthmus and formation of a thick endometrium which is difficult to be expelled through the cervix. Anovulatory cycles are painless due to absence of progesterone.
7. Prostaglandin effect is the most accepted theory. In primary dysmenorrhoea there is increased production of prostaglandin $F_{2\alpha}$ in the endometrium. It causes vasoconstriction and uterine ischaemia which may cause the pain of dysmenorrhoea. It also causes strong uterine contractions (uterine spasm). Progesterone stimulates the production of prostaglandins in the endometrium and so anovulatory cycles are painless. The production of prostaglandins reaches a peak at, or soon after, the start of menstruation. With the onset of bleeding, the formed prostaglandins are released from the shedding endometrium.

PGF₂ α also causes contraction of the gut musculature leading to nausea, vomiting, and diarrhoea reported by many women.

c. General Causes

1. Psychological disturbances. Pain may be an excuse to avoid school, work, etc. The disorder is frequent in girls whose mothers had the same complaint.
2. Smoking. This may release prostaglandins within the uterus.

Treatment

1. General Treatment

(a) Explanation and reassurance of the patient; (b) avoid sedentary life and encourage muscular exercises; (c) treatment of constipation and restriction of coffee; (d) yoga and acupuncture may be tried.

2. Nonhormonal Treatment

(a) Antispasmodics; (b) analgesics; (c) antiprostaglandins which inhibit the synthesis of prostaglandins as naproxen or ibuprofen (Brufen tablets 400 mg thrice daily during the period). Pain is relieved in 80% of cases.

3. Hormonal Treatment

Indicated when medical treatment fails. The main idea is to inhibit ovulation because anovulatory cycles are painless. Hormonal treatment is given for 6-12 successive months.

- a. Combined contraceptive tablets to inhibit ovulation. Pain is relieved in 90% of cases.
- b. The dydrogesterone compound Duphaston does not inhibit ovulation but relieves pain by reducing the strength of uterine contractions. One tablet (10 mg) is given twice daily for 21 days starting on 5th day of the cycle.

4. Surgical Treatment

Indicated when hormonal treatment fails.

- a. Dilatation of the cervix. The cervix is dilated to 10 mm (No 10 Hegar dilator). Excessive dilatation may be associated with incompetent cervix in a subsequent pregnancy. This cures 60% and improves 20% of cases. Dilatation acts as a local sympathectomy by causing laceration of the nerve fibres around the internal os which transmit pain, and by stretching the fibromuscular tissue at the internal os rendering it hypotonic. Sometimes after a period of relief lasting 6 months to 2 years, pain recurs due to regeneration of the nerve fibres. Dilatation can be repeated.
- b. Presacral sympathectomy (neurectomy). Indicated when all other measures fail. It is an abdominal operation to remove the presacral nerve or plexus of nerves lying in front of the 4th, 5th lumbar vertebrae and sacral promontory. About 80% are cured. Failure to obtain cure in every case is due to incomplete removal of the nerve tissue. Operation is done by laparotomy or laparoscopy.

- c. Laser uterine nerve ablation (LUNA). Through laparoscopy, laser is used to divide the uterosacral ligaments containing the nerve supply of the uterus. It is done alternative to presacral neurectomy.

MEMBRANOUS DYSMENORRHOEA

It is a rare type of spasmodic dysmenorrhoea in which pain is very severe and is relieved after the passage of an endometrial cast during the third or fourth day of menstruation. Typically, the cast is triangular in shape but sometimes, it is passed in the form of 2 or more large fragments.

Treatment is like spasmodic dysmenorrhoea in addition to repeated curettage to remove the unhealthy endometrium.

CONGESTIVE (SECONDARY) DYSMENORRHOEA

Aetiology

Pain is due to pelvic congestion which is caused by:

1. Chronic pelvic infection as cervicitis, endometritis or salpingitis.
2. Pelvic tumours as fibroids or ovarian cyst.
3. Abnormal position of the uterus as retroversion or prolapse.
4. Simple pelvic congestion due to chronic constipation or coitus interruptus.
5. Pelvic congestion syndrome due to broad ligament varicocele.
6. Endometriosis and adenomyosis lead to a specific type of dysmenorrhoea.
7. Extragenital lesions as chronic appendicitis.

Clinical Picture

Age

It usually occurs after the age of 30.

Parity

More in parous women.

Type of Pain

Pain starts several days (3-5 days) before the period, increases gradually as menstruation approaches and is relieved by the onset of the flow due to diminution of pelvic congestion. In some cases the pain is felt through the whole period. The pain is a continuous dull ache felt in the lower abdomen and accompanied with backache.

Associated Symptoms

Menorrhagia, polymenorrhoea and increased normal vaginal discharge (leucorrhoea) may occur.

Treatment

(1) Treatment of the cause; (2) analgesics; (3) measures to relieve pelvic congestion as ichthol in glycerine vaginal pessaries, warm vaginal douches and treatment of constipation. Ichthol is soothing for pain, and glycerine is hygroscopic and relieves congestion.

MITTELSCHMERZ OR OVULATION PAIN**CLINICAL PICTURE**

It is a midcycle dull aching pain felt in one or other iliac fossa about the time of ovulation. It lasts for a few hours rarely longer than 24 hours. Sometimes accompanied with nausea and vomiting. Pain may be severe and mistaken for appendicitis or acute abdominal conditions. Occasionally it is accompanied by increased vaginal discharge or slight vaginal bleeding (ovulation bleeding) which is due to a fall in the level of oestrogen at the time of ovulation.

AETIOLOGY

The pain may be due to:

1. Increased tension within the ovary due to a thickened tunica albuginea which interferes with rupture of the graafian follicle at the time of ovulation (preovulatory).
2. Peritonism. Irritation of the peritoneum by fluid or blood from the ruptured follicle (ovulatory).
3. Tubal contractions. The tube shows active contractions at the time of ovulation (prostaglandin effect) which may cause pain (postovulatory).

TREATMENT

(1) Explanation and reassurance; (2) analgesics; (3) temporary inhibition of ovulation by contraceptive tablets given for 3 months. Spontaneous cure is always liable to occur.

**PREMENSTRUAL SYNDROME
(OVARIAN CYCLE SYNDROME)****DEFINITION**

PMS means cyclic recurrence of psychological, behavioural, or somatic symptoms during the luteal phase of the menstrual cycle and in absence of organic disease. The symptoms are relieved by the end of menstruation. Symptoms occur only in ovulatory cycles. Symptoms must be severe enough to interfere with the woman's normal activities, and this differentiates PMS from premenstrual molimina.

PREVALENCE

It varies between 10 and 90%, however, severe PMS occurs in less than 10% of cases. This wide range of incidence is explained by the fact that more than 150 symptoms have been associated with PMS.

AGE INCIDENCE

It mostly occurs in women in their thirtieth and fortieth.

AETIOLOGY

The actual cause is unknown and the syndrome may be attributed to:

1. Endocrine Theory

- a. High oestrogen levels, or low progesterone levels, i.e., high oestrogen-progesterone ratio. Progesterone stimulates sodium loss thus preventing water retention, and has a sedative effect on the central nervous system.
- b. Allergic reaction to the corpus luteum so the syndrome is seen only with ovulatory cycles.
- c. Increased secretion of aldosterone which leads to salt and water retention.
- d. Increased antidiuretic hormone leading to water retention.
- e. Elevated serum prolactin.

2. Diet Theory

High intake of salt leading to water retention, low intake of refined sugar leading to hypoglycaemia, and magnesium deficiency.

3. Vitamin Theory

Deficiency of vitamin A, B₆, and E. Vitamin B₆ is a co-factor in the production of serotonin and dopamine.

4. Prostaglandin Theory

There is increased prostaglandin activity. Prostaglandins are produced in the brain, breast, gastrointestinal tract, kidney, and genital tract. These areas often present with symptoms in patients with PMS.

5. Endorphin Theory

There is a decrease in the level of beta-endorphins in the luteal phase. These endogenous opiates are associated with a sense of well-being. PMS symptoms mimic some symptoms of opiate withdrawal.

6. Serotonin Theory

Low serotonin level is associated with depression, while serotonin excess is associated with anxiety.

7. Psychological Disturbances

SYMPTOMS

1. Nervous symptoms: headache, migraine, palpitation, irritability, depression, insomnia, crying, and change in libido.
2. Behavioural symptoms as poor concentration, loss of motor skill, bad performance, hostility, and suicide attempts.

3. Gastrointestinal symptoms; as nausea, vomiting, diarrhoea, or constipation.
4. Mastalgia which means swelling and pain of the breasts.
5. Water retention manifested by oedema of the face, eyelids, and legs, and temporary increase in body weight.
6. Hypoglycaemia-like symptoms; as increased appetite, craving for sweets, and fatigue.
7. Pain in the form of backache and cramps.
8. Worsening of medical conditions as asthma, epilepsy, migraine, and rheumatoid arthritis.

DIAGNOSIS

It depends on the presence of symptoms which are related to the luteal phase of the cycle. Symptoms must be absent during the follicular phase. Physical examination and laboratory tests do not show abnormal findings. However, a complete physical examination must be done to exclude an organic cause that might be responsible for the symptoms.

TREATMENT

1. Explanation and reassurance.
2. Moderate exercise may be helpful by increasing production of endogenous endorphins.
3. Diet. Increase the carbohydrate intake by giving refined sugar to prevent hypoglycaemia-like symptoms and give primrose oil. Restriction of salt for 7-10 days premenstrually to reduce fluid retention. Reduce caffeine intake.
4. Diuretics. Given for symptoms of water retention. Spironolactone (Aldactone) is the diuretic of choice (100 mg daily). It inhibits aldosterone secretion.
5. Symptomatic treatment. Tranquilizers for irritability and antidepressants as fluoxetine (Prozac – 20 mg daily).
6. Progestogens. To improve luteal phase deficiency. Progesterone suppositories are inserted vaginally or rectally; 200-400 mg twice daily, or a progestogen oral tablet as norethisterone (Primolut-N) is given.
7. Dopamine agonists. Bromocriptine (Parlodel) or lisuride (Dopergin) tablets to inhibit prolactin secretion. It is tried if the main complaint is mastalgia. The dose of bromocriptine is one tablet (2.5 mg) twice daily.
8. Vitamin B₆ (pyridoxine). It increases the synthesis of dopamine which is the prolactin-inhibiting hormone (100 mg daily). It also increases the synthesis of serotonin.
9. Anti-prostaglandins. Effective in patients with headache, backache, cramps and mastalgia.
10. Danazol. It relieves mastalgia. It is considered only when other drugs have failed because it has many side effects.

Generally, the drugs are started 10-14 days before the period. Sometimes a combination of therapy is useful.

11. Inhibition of ovulation. This is the most appropriate treatment and is achieved by:
 - a. Combined oral contraceptives.
 - b. Oestradiol implants.

- c. Oestradiol skin patches.
 - d. Depo-Provera (medroxyprogesterone acetate) 150 mg IM every 3 months.
 - e. Gonadotrophin releasing hormone analogues (agonists). These lead to amenorrhoea, anovulation, and drop in oestrogen level (medical oophorectomy).
 - f. Mifepristone. It blocks ovulation and reduces the symptoms.
12. Psychotherapy for resistant cases.

AMENORRHOEA

Amenorrhoea means absence of menstruation.

TYPES

1. Primary amenorrhoea means failure of menstruation to occur by the age of 14 years in the absence of the secondary sex characters, or by the age of 16 years in the presence of secondary sex characters. The incidence is <1%.
2. Secondary amenorrhoea means cessation of menstruation for 3 months, if previous menses were regular, and for 6 months, if previous menses were infrequent. The incidence is 0.7%.

Note. Delayed menarche means spontaneous onset of menses in a woman older than 16 years who has no reproductive abnormalities.

AETIOLOGY

Amenorrhoea may be physiological or pathological.

Causes of Physiological Amenorrhoea

1. Before puberty due to a low secretion of gonadotrophin releasing hormone (GnRH).
2. After menopause due to disappearance of all ovarian follicles, so the ovaries will not respond to the pituitary gonadotrophins.
3. During pregnancy because of continuous production of large amounts of oestrogen and progesterone without withdrawal. Pregnancy is the commonest cause of secondary amenorrhoea.
4. Lactation. Prolactin inhibits the production of gonadotrophin releasing hormone and renders the ovary refractory to the action of pituitary gonadotrophins. It also inhibits ovarian steroidogenesis.
5. Periods of amenorrhoea may occur shortly after menarche due to immaturity of the hypothalamic-pituitary-ovarian axis or before menopause due to decreased number of ovarian follicles and their increased resistance to gonadotrophin stimulation.

Pathological Amenorrhoea

This may be false or true.

False Amenorrhoea "Cryptomenorrhoea"

In this condition, menstruation occurs but the blood is unable to escape due to the presence of obstruction in the genital tract as cervical stenosis, transverse vaginal septum, vaginal aplasia, and imperforate hymen. Cervical stenosis may be congenital or acquired after amputation or cauterization of the cervix.

Aetiology of True Pathological Amenorrhoea

I. General Causes

(1) Malnutrition; (2) voluntary weight loss (dieting); (3) obesity; (4) any acute illness can cause a short period of amenorrhoea; (5) chronic diseases as diabetes mellitus, pulmonary tuberculosis and chronic nephritis; (6) drugs as androgen and contraceptive pills; (7) hypercarotinaemia may cause amenorrhoea, cause is unknown. The ovaries are stained with the yellow carotene pigment (golden ovaries). Other tissues as the skin may be stained yellow; (8) jogger's amenorrhoea, seen frequently in women training for marathon racing and other forms of violent exercises. There is increased secretion of beta-endorphins and prolactin which inhibit the pulsatile release of GnRH.

Note. A certain amount of body fat is needed to have normal regular menstruation (Frisch theory). Suboptimal and supraoptimal amount of fat may impair oestrogen metabolism and leads to amenorrhoea. The weight usually needs to be more than 45 kg for menstruation to occur.

II. Hypothalamic Amenorrhoea

1. Organic lesions; traumatic, inflammatory as meningitis and encephalitis, or neoplastic.
2. Psychological disturbances as marked sorrow, war amenorrhoea, and change of environment.
3. False pregnancy "pseudocyesis". See Obstetrics.
4. Anorexia nervosa.
5. Bulimia.
6. Frolich syndrome.
7. Laurence-Moon-Biedl syndrome.
8. Isolated gonadotrophin releasing hormone deficiency and Kallmann syndrome.
9. Mental disorders as schizophrenia.
10. Electroconvulsive therapy.
11. Drugs as phenothiazines and methyldopa (Aldomet) lead to hyperprolactinaemia and amenorrhoea. These drugs inhibit the secretion of dopamine.
12. Postpill amenorrhoea.
13. Functional hypothalamic amenorrhoea. It is supposed to be due to absence or reduced frequency of GnRH pulse leading to decreased production of FSH and LH. However, we cannot test the hypothalamus to prove this diagnosis which is made after excluding all other causes of amenorrhoea.



Note. Dopamine is the prolactin-inhibiting hormone or factor (PIH or PIF). Decreased secretion leads to hyperprolactinaemia.

III. Pituitary Amenorrhoea

1. Pituitary infantilism (Lorain syndrome).
2. Pituitary cachexia known as Simmonds disease or Sheehan syndrome.
3. Pituitary tumours: basophil adenoma leading to Cushing disease, acidophil adenoma leading to gigantism or acromegaly, and prolactinoma.
4. Craniopharyngioma. It arises from Rathke pouch. It causes pressure atrophy of the gonadotrophin secreting cells.
5. The empty sella syndrome.

IV. Disorders of the Thyroid Gland

Hypo- or hyperthyroidism may cause menstrual abnormalities including amenorrhoea. The mechanism of which is not clear.

V. Disorders of the Adrenal Glands

1. Hypofunction or Addison disease.
2. Hyperfunction due to hyperplasia, adenoma or carcinoma as in Cushing syndrome and congenital adrenal hyperplasia.

VI. Ovarian Amenorrhoea

- (1) Gonadal dysgenesis including Turner syndrome; (2) the polycystic ovary syndrome; (3) destruction of both ovaries by radium, deep x-ray, chemotherapy, tuberculosis or carcinoma; (4) surgical removal of both ovaries; (5) virilizing ovarian tumours as androblastoma; (6) metropathia haemorrhagica; (7) persistent corpus luteum (Halban disease); (8) premature ovarian failure; (9) resistant ovary syndrome.

VII. Uterine Amenorrhoea

1. Absence of uterus; congenital or surgical removal.
2. Severe degree of hypoplasia.
3. Overcurettage removing the basal layer of endometrium.
4. Destruction of the endometrium by radium, tuberculosis, gangrenous endometritis occurring after abortion or labour.
5. Asherman syndrome or intrauterine adhesions occurring after curettage or infection (amenorrhoea traumatica).

VIII. Chromosomal Causes

As Turner syndrome (45 XO), superfemale (47 XXX) and testicular feminization (46 XY).

IX. Idiopathic Amenorrhoea. No cause can be detected.

DIAGNOSIS OF AMENORRHOEA

A. History

1. Personal history. (a) Age of the patient to exclude menopause; (b) marital state to exclude pregnancy.
2. Menstrual history. To know the type of amenorrhoea whether primary or secondary and its duration.
3. Obstetric history particularly for Sheehan syndrome.
4. Past history of chronic diseases as diabetes mellitus and tuberculosis, of operation on the genital tract as curettage, irradiation and previous intake of drugs and contraceptive tablets.
5. Family history of diabetes mellitus, tuberculosis, testicular feminization and polycystic ovary syndrome.
6. Present history. The presence of other symptoms as obesity, wasting, anosmia, galactorrhoea, psychological disturbances and hot flushes indicating premature menopause. Symptoms suggestive of pregnancy.

B. General Examination

1. Absence of secondary sex characters (breast development, axillary and pubic hair).
2. Signs of anaemia and general disease as tuberculosis.
3. Presence of hirsutism or virilization.
4. The presence of obesity or wasting. The body mass index is calculated.
5. The height, weight, and span are determined.
6. Examination of the thyroid, chest, and breasts and galactorrhoea is excluded by squeezing all quadrants of both breasts.
7. Examination of urine for sugar, protein and casts (for diabetes mellitus and chronic renal disease).

C. Abdominal Examination

For a pelvi-abdominal mass as pregnancy or haematocolpos.

D. Local Examination

To know the condition of vulva, clitoris, vagina, cervix, uterus, ovaries and the presence of pelvic masses.

E. Special Investigations

If the history and clinical examination do not reveal a cause the following tests are carried out as a routine: (a) progestogen challenge test; (b) estimation of serum FSH, LH, TSH, and prolactin. Hyperprolactinaemia is responsible for 20% of cases of secondary amenorrhoea.

Progestogen Challenge Test

Progesterone causes uterine bleeding if the endometrium has been primed with oestrogen. A progestogen as norethisterone, 5 mg tablet is given twice daily for five days. If withdrawal bleeding occurs (within 2 weeks usually after 2 to 7 days) it means that the ovary is producing oestrogen alone but not progesterone i.e. anovulation. If no bleeding occurs it means either the ovary is not producing oestrogen or the uterus is not responding as in case of intrauterine adhesions. In this case an oestrogen-progestogen challenge test is carried out. A combined oral contraceptive pill is given for three weeks. If no bleeding occurs this means a uterine cause of amenorrhoea. However, if bleeding occurs the fault is in the ovary and this ovarian failure may be primary in the ovary or secondary to pituitary failure.

Serum FSH and LH

(a) A high serum level of FSH (above 40 mIU/ml) indicates ovarian failure and that the ovary is not producing oestrogen; (b) low serum FSH (less than 5 mIU/ml) indicates a hypothalamic or pituitary problem; (c) an LH:FSH ratio 2 or more is diagnostic of polycystic ovarian disease.

Other investigations are done according to the history and clinical examination and include:

1. Investigations for uterine amenorrhoea:
 - Pregnancy test if pregnancy is suspected.
 - A uterine sound is passed to diagnose uterine hypoplasia.
 - Ultrasonography diagnoses uterine hypoplasia and Asherman syndrome.
 - Hystero-grography or hysteroscopy diagnoses Asherman syndrome.
 - Uterine curettage to diagnose tuberculous endometritis.
2. Investigations for ovarian amenorrhoea:
 - Ultrasonography diagnoses polycystic ovaries, streak gonads or a small ovarian tumour.
 - Laparoscopy may show a small ovarian tumour, streak gonads or polycystic ovaries.
3. Investigations for the adrenal glands:
 - Estimation of serum cortisol and ACTH to diagnose Cushing syndrome.
 - Serum 17α -hydroxyprogesterone to diagnose congenital adrenal hyperplasia.
 - Computed tomography (CT) scan or magnetic resonance imaging (MRI) to exclude adrenal tumour.
4. Thyroid function tests for thyroid disorders.
5. Investigations for pituitary amenorrhoea:

If a pituitary tumour is suspected, we examine the retina and visual fields and do a CT scan or MRI which is more accurate but more expensive.
6. Glucose tolerance test if we suspect diabetes mellitus.

7. Chromosomal study must be done in every case of primary amenorrhoea as about 40% of these cases show chromosomal anomalies.

TREATMENT OF AMENORRHOEA

1. General Treatment

- (a) Proper diet, correction of malnutrition and obese patients are advised to lose weight;
- (b) psychotherapy if necessary.

2. Treatment of the Cause

Examples include control of diabetes mellitus, treatment of tuberculosis, and removal of a virilizing ovarian tumour. Hyperprolactinaemia is treated by a dopamine agonist as bromocriptine (Parlodel) or lisuride (Dopergin). Hypothyroidism is treated by thyroxine.

3. Hormonal Treatment

It is indicated in absence of an organic cause i.e. dysfunctional amenorrhoea.

- a. Cyclical treatment with oestrogen followed by progestogen like the normal cycle. The treatment is given for 3 successive months. This may be followed by restoration of normal cycles.
- b. Induction of ovulation. Clomiphene (Clomid) and gonadotrophins are only used if the patient is complaining of infertility. These drugs cause ovulation and menstruation. The gonadotrophin releasing hormone given intravenously or subcutaneously in a pulsatile fashion every 60-90 minutes using a computerized pump, can cause ovulation and menstruation if there is a hypothalamic dysfunction.

PRIMARY AMENORRHOEA

Aetiology

- A. False amenorrhoea or cryptomenorrhoea. Due to congenital cervical stenosis, transverse vaginal septum, vaginal aplasia or imperforate hymen.
- B. True amenorrhoea. The causes are:
 - I. Hypothalamic amenorrhoea:
 - (1) Organic lesions; traumatic, inflammatory or neoplastic; (2) Frolich syndrome; (3) Laurence-Moon-Biedl syndrome; (4) isolated gonadotrophin-releasing hormone deficiency and Kallmann syndrome.
 - II. Pituitary amenorrhoea:
 - (1) Pituitary infantilism (Lorain syndrome); (2) gigantism due to acidophil adenoma; (3) empty sella syndrome.
 - III. Hypothyroidism.
 - IV. Disorders of the adrenal glands:
 - (1) Addison disease occurring in a young girl; (2) congenital adrenal hyperplasia.

V. Ovarian amenorrhoea:

(1) Gonadal dysgenesis including Turner syndrome and pure gonadal dysgenesis: (2) the polycystic ovary syndrome may present with primary amenorrhoea.

VI. Uterine amenorrhoea:

(1) Congenital absence as in Mayer-Rokitansky-Kuster-Hauser syndrome; (2) severe degree of hypoplasia.

VII. Hyperprolactinaemia.

VIII. Chromosomal causes:

These are responsible for about 40% of cases of primary amenorrhoea and include gonadal dysgenesis, superfemale, and testicular feminization. Gonadal dysgenesis is the commonest cause of primary amenorrhoea and accounts for about 30% of all cases.

IX. True hermaphrodite.

Note. The most common cause of primary amenorrhoea is constitutional delay, so the ages of menarche of the mother and any sister should be determined.

OLIGO- AND HYPOMENORRHOEA

Oligomenorrhoea means infrequent menstruation, so the length of the cycle is more than 35 days.

Hypomenorrhoea means scanty menstruation (less than 30 ml) or the duration of the flow is less than 2 days.

Oligo- and hypomenorrhoea often occur together.

Note. Absence of menstruation for 3 months or more is considered amenorrhoea and not oligomenorrhoea.

Aetiology

1. Constitutional oligohypomenorrhoea. It is present from the menarche. The patient is normal, the cycles are ovulatory and it requires no treatment.
2. Pathological type. The aetiology and treatment are like that of amenorrhoea.

SYNDROMES ASSOCIATED WITH AMENORRHOEA

Frolich Syndrome

It is a hypothalamic disturbance occurring from childhood. There is obesity, infantile genital organs, primary amenorrhoea, and sleepiness. The Laurence-Moon-Biedl syndrome has similar features but in addition there is retinitis pigmentosa, mental deficiency and polydactyly. Obesity affects the shoulder girdle, the breasts, the pelvic girdle and thighs.

Anorexia Nervosa

It is due to psychological disturbance affecting the hypothalamus and appetite. There is amenorrhoea, emaciation, weakness, hypoglycaemia, low basal metabolic rate and subnormal

temperature. FSH, LH, oestrogen, T_3 and T_4 are low. Treatment by psychotherapy. Ovulation induction is possible with clomiphene and pulsatile GnRH in patients wishing to conceive.

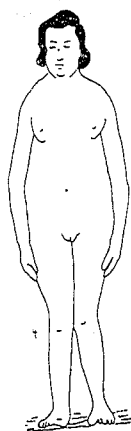


Fig.19. Frolich syndrome

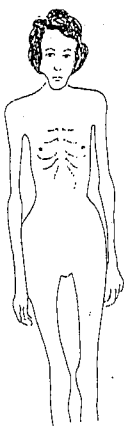


Fig.20. Anorexia nervosa



Fig.21. Cushing syndrome

Bulimia

The syndrome is marked by episodes of overeating followed by self-induced vomiting, fasting, or the use of laxatives and diuretics to avoid gain in weight. The patient usually has depressive symptoms with menstrual irregularities and amenorrhoea of hypothalamic origin. However, the patient may not develop amenorrhoea. Treated by behavioural therapy.

Kallmann Syndrome

Anosmia or hyposmia, infantile genital organs, and primary amenorrhoea due to isolated deficiency of GnRH. Sometimes this isolated deficiency is associated with other congenital abnormalities as colour blindness. Treatment is by cyclic oestrogen and progestogen to stimulate growth of the breasts, to induce menstruation, and to prevent osteoporosis.

Postpill Amenorrhoea (Shearman Syndrome)

Oral contraceptives inhibit ovulation by inhibiting the hypothalamic-pituitary axis leading to suppression of FSH and LH. Occasionally this suppression persists for several months after stopping the oral contraceptive producing postpill amenorrhoea. This occurs in less than 1% of cases, and is not related to the length of intake of the pill. This suppression resolves spontaneously and does not last more than 6 months. So if amenorrhoea lasts more than 6 months the case is investigated to determine the cause.

Pituitary Infantilism of Lorain

The physical and sexual development are arrested so there is dwarfism and hypogonadism. Only the production of the growth hormone and gonadotrophins is affected. The cause is unknown.

Pituitary Cachexia (Panhypopituitarism)

In Simmonds disease there is destruction of the anterior lobe of pituitary due to any cause in either sex e.g. septic embolic due to postpartum infection. In Sheehan syndrome there is spasm and thrombosis of the anterior pituitary arterioles due to severe postpartum haemorrhage, so it occurs only in females. This leads to hypogonadism, hypothyroidism, and adrenocortical insufficiency, so there is atrophy of the breasts and genital organs, amenorrhoea and failure of lactation (deficiency of prolactin) after delivery. Absence of lactation is the first sign. Other manifestations include falling of hair, hypotension, hypoglycaemia, weakness and loss of weight with pale waxy skin (deficiency of melanocyte stimulating hormone). More than 75% of the anterior pituitary has to be destroyed to produce symptoms of deficiency. Treatment by cortisone and thyroxine for life. Oestrogen-progestogen therapy is given to induce menstruation. If pregnancy is desired we give gonadotrophins.

Note. The posterior lobe of the pituitary gland is not affected by severe postpartum haemorrhage as blood is shifted from the anterior lobe to the posterior lobe during labour as the latter is active and secretes oxytocin and so it is not affected by ischaemia.

The Empty Sella Syndrome

It is a congenital condition due to herniation of the subarachnoid space into the sella turcica (pituitary fossa). The syndrome can also occur secondary to surgery, radiotherapy or infarction of a pituitary tumour. The hernial sac containing cerebrospinal fluid will lead to compression of the pituitary gland and enlargement of the fossa. It may lead to amenorrhoea and is sometimes associated with hyperprolactinaemia. It is diagnosed only by CT or MRI which is more accurate.

Cushing Syndrome

The clinical picture is due to hyperfunction of the adrenal cortex. It is characterized by amenorrhoea, hirsutism, acne, trunkal obesity, muscle wasting and weakness, moon face, striae of the skin, hypertension, hyperglycaemia, osteoporosis, and polycythaemia.

Aetiology

1. Pituitary Cushing syndrome; due to basophil adenoma leading to over production of ACTH and subsequent bilateral adrenal hyperplasia. Usually called Cushing disease. Treated by trans-sphenoidal removal of the tumour and/or deep x-ray therapy.
2. Adrenal Cushing syndrome; due to adenoma or carcinoma of the adrenal gland. Excessive production of cortisol results in complete suppression of ACTH secretion and atrophy of the contralateral adrenal gland. The lesion is usually bilateral. Treatment is bilateral adrenalectomy and cortisol for life.
3. Hypothalamic Cushing syndrome. There is excessive production of ACTH in absence of pituitary tumour. The disorder is in the hypothalamus.
4. Ectopic Cushing syndrome. Some malignant tumours as lung cancer may produce ACTH.

Note. The adrenal cortex produces corticosteroids, mineralosteroids, and sex hormones (androgen and oestrogen).

Congenital Adrenal Hyperplasia. See intersex.

Gonadal Dysgenesis

It means failure of the gonad to develop and will be in the form of fibrous bands "streak gonads." Two syndromes are described.

1. Turner Syndrome

This is the commonest type of gonadal dysgenesis. The chromosomal arrangement is 45XO or mosaic 45XO-46XX, or 45XO-46XY. Turner syndrome is characterized by physical abnormalities, so the patient is short (<150 cm) with webbing of the neck (50%), shielding of the chest, coarctation of the aorta, cardiac and renal abnormalities, cubitus valgus, deformities of the ears, fingers, and toes. The breasts remain underdeveloped with widely spaced nipples, and the genital organs are infantile. The ovaries are in the form of fibrous bands with no follicles i.e.

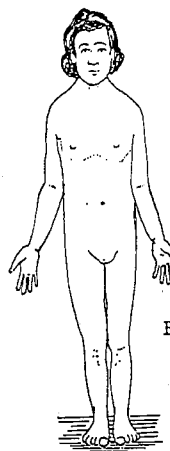


Fig.22. Turner syndrome

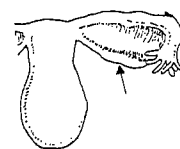


Fig.23. Streak gonads

streak gonads. There is primary amenorrhoea. Because the ovaries are inactive the oestrogen level is low and FSH and LH levels are high (hypogonadotropic hypogonadism). Treatment is by cyclic oestrogen and progestogen to stimulate growth of the breasts, to induce menstruation and to prevent osteoporosis. Oestrogen is not given alone as it may cause endometrial carcinoma. We can give conjugated oestrogens (Premarin), 0.625 mg daily and medroxyprogesterone acetate (Provera tablets), 5-10 mg daily for 10-14 days each month. Treatment is started when bone age is greater than 13 years to avoid early closure of bone epiphyses. To increase final height, growth hormone can be given before starting oestrogen therapy. It increases height by about 8 cm. If the karyotype is mosaic with Y chromosome, the streak gonads are testicles and should be removed as early as possible, as the risk of malignancy is high about 25%, because the gonad is abnormal in structure. Pregnancy can be achieved in Turner syndrome using donated oocytes (condemned in Moslem countries).

Notes for the postgraduate

1. Loss of genes on the short arm of one X chromosome leads to the short stature and physical abnormalities of Turner syndrome. Loss of genes on the long arm of one X chromosome leads to streak gonads and primary amenorrhoea.
2. Some mosaic cases of Turner syndrome with karyotype 45XO-46XX have functioning ovaries due to the presence of normal cells (46XX). These patients may appear as normal females. On

rare occasions they menstruate and may even become pregnant. However, they are liable to have premature ovarian failure leading to premature menopause.

3. Bone age is determined by x-ray examination of the hand and wrist and compared with a standard for patient age. The nondominant hand is used for x-ray examination.
4. Noonan (or Ulrich) syndrome. Affects males and females. Normal chromosomes, normal gonads but with physical abnormalities of Turner syndrome. The patient is fertile.
5. Turner syndrome is the commonest chromosomal abnormality occurring in females. It has increased incidence of hypertension, diabetes, deafness, and colour blindness (red and green).

2. Pure Gonadal Dysgenesis

The patient has streak gonads, infantile breasts and genital organs, and primary amenorrhoea. She is often taller than normal and does not show the physical abnormalities of Turner syndrome. The karyotype is 46XX or 46XY. When the karyotype is 46 XY, the condition is termed Swyer syndrome. Treated in the same way as Turner syndrome.

Polycystic Ovary Syndrome (PCOS)

The syndrome was first described by Stein and Leventhal in 1935, and the old name was Stein-Leventhal syndrome.

Prevalence

About 5-10% of women in the reproductive age have PCOS.

Aetiology

The syndrome is due to hyperandrogenism which is due to one or more of the following factors:

1. Hypothalamic and/or pituitary abnormality in the form of increased LH secretion. LH stimulates the theca cells of the ovary to produce androgens.
2. Genetic deficiency of the aromatase enzyme which is necessary for the conversion of ovarian androgens to oestrogens. Some patients – but not all – show familial tendency to develop the syndrome (mother or sister). In fact about 50% of first degree relatives have PCOS.
3. Hyperinsulinaemia, due to increased peripheral resistance to insulin. It is present in about 50% of cases, and affects both obese and nonobese patients. It leads to hyperandrogenism which is explained by: (a) decrease in the hepatic synthesis of sex-hormone binding globulin, and this increases free testosterone, and free oestradiol; (b) inhibition of hepatic synthesis of insulin growth factor-1 (IGF-1) binding globulin leading to increased free IGF-1. This factor increases the sensitivity of theca cells in the ovary to the action of LH; (c) increased production of IGF-1 in the ovary; (d) increased secretion of dehydroepiandrosterone sulphate (DHEAS) from the suprarenal gland.
4. Suprarenal abnormality may lead to overproduction of suprarenal androgens.

In fact, the excess androgens come from the ovaries or from the ovaries and suprarenal glands.

Clinical Picture

Most cases occur between the ages of 17 and 30 years. Patient complains of one or more of the following:

1. Menstrual abnormalities in the form of primary or secondary amenorrhoea, oligomenorrhoea, occasionally menorrhagia, or irregular uterine bleeding. In many patients, the menstrual disturbance dates from menarche. It is the commonest presenting feature (80%).
2. Infertility due to anovulation.
3. Obesity in about 50% of patients.
4. Hirsutism in 60-80% of patients in USA and in 10-20% of Japanese patients.
5. Male alopecia and acne vulgaris.
6. Acanthosis nigricans. It is a gray-brown discoloration of the skin usually affecting the neck, axillae, under the breasts, groin, and vulva. It is due to hyperinsulinaemia.

Pathology

1. Ovaries. Both ovaries are enlarged 2-3 times the normal size and are cystic. The tunica albuginea is thick, smooth, white, and does not show the indentations of the normal ovary (porcelain ovaries or ping-pong ball appearance). There is no ovulation as the follicles do not rupture and become cystic. There are multiple small subcapsular cystic follicles (microcysts) which are filled with clear fluid rich in androgens. There is hyperplasia of the theca interna cells around the cystic follicles. This hyperthecosis is due to increased secretion of luteinizing hormone (LH) and the cells are often luteinized. The metabolism in the ovary is disturbed with increased production of androgens in the form of testosterone, androstenedione, and dehydroepiandrosterone (DHEA).
2. Endometrium. It is proliferative or hyperplastic due to unopposed oestrogen (anovulation and absence of progesterone). It may be atrophic due to excess androgens.

Hormonal Profile

(1) Increased LH in about 40% of cases; (2) normal or low FSH; (3) increased LH:FSH ratio to be 2 or more; (4) increased oestrone and free oestradiol; (5) increased androgens: testosterone (in 70%), androstenedione (in 50%), and DHEA. Dehydroepiandrosterone sulphate (DHEAS) which comes from adrenal glands (almost 100%) is raised in about 50% of cases; (6) fasting serum insulin is increased in about 50% of cases.

The serum FSH and LH are measured on day 2, 3, or 4 of the menstrual cycle to have a basal secretion of both hormones. At this time, LH is considered high if it is >10 mIU/ml and FSH is considered normal if it is <10 mIU/ml.

Key Points

1. Oestrone is increased due to increased peripheral conversion of androstenedione into oestrone in body fat.

2. High oestrone level leads to increased secretion of LH and decreased that of FSH.
3. Increased LH secretion causes hyperplasia of the theca interna cells (hyperthecosis) and increased production of androgens.
4. Increased testosterone leads to thickening of the tunica albuginea and atresia of ovarian follicles.
5. Obesity reduces hepatic synthesis of sex-hormone binding globulin (SHBG) and increases free testosterone and free oestradiol.
6. Obesity and hyperandrogenism lead to increased insulin resistance.
7. There is relative excess of LH to FSH, and this leads to failure of ovulation. FSH is necessary for the development of the mature graafian follicle.
8. Ovarian androgens are secreted mainly from the theca interna cells, but also from ovarian stroma cells.

Diagnosis

1. Diagnosis is easily made by the clinical picture alone.
2. Hormonal profile.
3. Glucose tolerance test which is impaired in some cases, fasting serum insulin is measured to diagnose hyperinsulinaemia (normal 10-20 U/ml), and fasting glucose: fasting insulin ratio is determined to diagnose increased insulin resistance. A ratio less than 4.5 is abnormal and indicates increased insulin resistance.
4. Sonography. It shows the presence of 12 or more cystic follicles (microcysts) in each ovary and/or ovarian volume more than 10 cm³. The microcysts are 2 to 10 mm in diameter and are arranged either peripherally under the capsule giving a necklace-like appearance or they are scattered throughout the ovarian stroma. The increase in the stroma volume increases the production of androgens. Doppler ultrasound shows increased blood flow to the stroma.
5. Laparoscopy. When done in case of infertility it diagnoses the polycystic ovaries.

Note. 10-25% of normal women with regular cycles show polycystic ovaries without the clinical features of PCOS. Also about 15% of women on oral contraceptives show the ultrasound findings typical of PCOS.

Complications of PCOS

1. Menstrual abnormalities.
2. Infertility due to anovulation.
3. Hirsutism.
4. Increased risk of endometrial carcinoma due to anovulation and absence of progesterone resulting in unopposed oestrogen action. There is also increased risk of ovarian carcinoma.
5. Patient may develop type II diabetes mellitus due to increased insulin resistance.

6. Increased risk of hypertension and coronary heart disease. Both hyperinsulinaemia and hyperandrogenism increase the low-density lipoproteins and triglycerides and lower the high-density lipoproteins.
7. During pregnancy, there is increased incidence of abortion, and gestational diabetes.

Treatment

I. General Treatment

1. Obese women should lose weight. Obesity reduces SHBG and increases free testosterone. It leads to increased insulin resistance and hyperinsulinaemia. It also increases LH level by increasing peripheral oestrogen production. Loss of weight produces opposite effects.
2. Smoking is stopped as it may increase the adrenal androgens.

II. If the Patient Does Not Desire Pregnancy

1. A progestogen is given for 10 days each month to regulate the menstrual cycle and prevent endometrial hyperplasia resulting from unopposed oestrogen. Medroxyprogesterone acetate tablets (Provera tablets), 10 mg daily for 10 days each month.
2. The use of a combined oral contraceptive. It produces the above mentioned effects.
3. In case of hirsutism we give a combined oral contraceptive which has no or little androgenic effects as Diane tablets and the new contraceptive tablets containing third-generation progestogens, e.g. Marvelon or Gynera tablets. Other drugs are also used for treatment of hirsutism.

III. If the Patient Desires Pregnancy

The treatment will be medical, surgical, or assisted reproductive techniques.

1. Medical Treatment

The following drugs are used to induce ovulation:

- a. Clomiphene citrate (Clomid).

If clomiphene therapy fails to induce ovulation, one of the following is tried:

1. Clomiphene + human chorionic gonadotrophin (HCG).
2. Clomiphene + dexamethasone, if the patient is having a high level of dehydro-epiandrosterone sulphate (DHEAS) which is secreted by the adrenal glands. Dexamethasone, 0.5 mg orally at bedtime to inhibit the ACTH peak which occurs during sleep.
3. Letrozole (Femara). The dose is 2.5 mg daily for 5 days starting on third day of cycle. When the ripe follicle reaches 18 mm or more in diameter HCG is given. The drug inhibits peripheral oestrogen production (aromatase inhibitor). This leads to increased FSH which is necessary for the development of the mature graafian follicle. The drug can be combined with clomiphene.
4. Gonadotrophins + HCG.
5. Gonadotrophin releasing hormone given in a pulsatile manner.



- b. Insulin sensitizing agents. Some oral hypoglycaemics can be given if there is hyperinsulinaemia. These drugs reduce insulin resistance, insulin secretion, and secretion of androgens. They can induce ovulation and lead to pregnancy. If treatment fails they are combined with clomiphene. The dose of metformin (Glucophage) is 500 mg 2 or 3 times daily, given for 6-12 months.

Note. Gonadotrophins include human menopausal gonadotrophins, urinary FSH, and recombinant FSH.

2. Surgical Treatment

Indicated when medical treatment fails to induce ovulation, and it may be done alternative to stimulation with gonadotrophins which carries the risk of ovarian hyperstimulation, multiple pregnancy and its complications, and the need for intensive monitoring of the patient during stimulation.

Surgical treatment is by ovarian drilling. Diathermy coagulation of the ovaries is done using the laparoscope. The strength of the current, time of application, and number of points to be cauterized are not standardized. Some use a current of 40 watts for 4 seconds to cauterize 4 points in each ovary. LASER may be used for ovarian drilling (YAG, carbon dioxide, or KTP LASER). The rate of ovulation is about 70-80%, and rate of pregnancy is about 40%. Complications of drilling include pelvic adhesions. Also destruction of ovarian tissue may be followed by premature ovarian failure and possible ovarian cancer.

Notes

- Wedge resection of both ovaries is no more done as it may be followed by periovarian and peritubal adhesions which prevent pregnancy.
- Drilling destroys ovarian stroma and so reduces androgen production.

3. Assisted Reproductive Techniques

Resorted to if all measures fail to achieve pregnancy. These include intrauterine insemination, in Vitro Fertilization and Embryo Transfer.

Note. The rate of abortion is high (25-40%) in women with PCO who become pregnant. This may be due to a high level of LH in the follicular phase. This leads to early meiosis and an aged oocyte (abnormal ovum). Also during pregnancy, there is increased incidence of gestational diabetes mellitus.

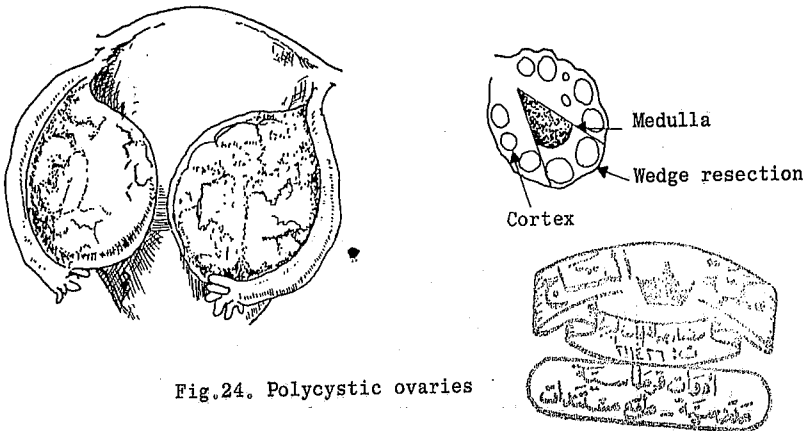


Fig.24. Polycystic ovaries

Resistant Ovary Syndrome (Savage Syndrome)

It is confined to women below 35 years of age. For some unknown reason the ovary fails to respond to pituitary gonadotrophins. This may be due to lack of sensitivity, absence, or decreased number of gonadotrophin receptors on the ovarian follicles. This leads to high levels of FSH and LH and low oestrogen level. The ovaries show normal number of follicles. The condition is only diagnosed by ovarian biopsy to differentiate it from premature ovarian failure. The biopsy should include the full thickness of the ovary as the normal follicles may be deeply located in the ovarian stroma. Some cases may recover spontaneously and get pregnant. Treatment is by repeated induction of menstruation with cyclic oestrogen-progestogen therapy and this may be followed by spontaneous recovery. If the patient wants to conceive, large doses of gonadotrophins are tried, however, the chance of pregnancy is very poor. Also ovum donation can be tried, however, this is condemned in Moslem countries.

Asherman Syndrome (Amenorrhoea Traumatica)

Aetiology

Intrauterine adhesions (IUA-synechiae) may occur as a result of:

1. Excessive uterine curettage after abortion (commonest cause), postpartum, diagnostic and therapeutic curettage.
2. Uterine infection; postabortive, postpartum, tuberculous, and bilharzial infection.
3. Myomectomy and caesarean section.
4. After insertion of intrauterine contraceptive device, and radium.

Classification of IUA by Hysteroscopic Findings

1. Minimal degree. Less than one-fourth of the uterine cavity involved by adhesions.
2. Moderate degree. One-fourth to three-fourths of uterine cavity involved by adhesions.
3. Severe degree. More than three-fourths of uterine cavity involved by adhesions.

Symptoms

Slight adhesions are not associated with symptoms. However, the patient may complain of hypomenorrhoea, amenorrhoea, dysmenorrhoea, and infertility (most common symptom). Hypomenorrhoea, and amenorrhoea are due to reduction in the surface area of the bleeding endometrium, as the endometrium is replaced by fibrous tissue. Infertility is due to mechanical obstruction in the cervical canal and uterine cavity preventing ascent of spermatozoa, or the poor decidual reaction in the endometrium interfering with implantation of the ovum. During pregnancy, the patient may complain of repeated abortion (lack of space in the uterine cavity), preterm labour, placenta praevia, and placenta accreta as the decidua basalis is absent or poorly formed due to over curettage.

Note. Obliteration of the region of the uterine isthmus by adhesions leads to reflex inhibition of the endometrium and amenorrhoea, but not cryptomenorrhoea.

Diagnosis

1. History of operation on the uterus or uterine infection.
2. In some cases the external os of the cervix is reduced to a very small hole or completely stenosed. If a uterine sound is passed it shows a limited mobility inside the uterus.
3. Negative progesterone and oestrogen-progesterone challenge tests in the presence of normal levels of FSH and LH (refractory endometrium).
4. Adhesions are seen by hystero-graphy (filling defects), sonography, or by hysteroscopy which is more accurate as it detects minimal adhesions which do not appear on hystero-gram.

Treatment

Adhesions are divided blindly by dilatation and curettage, or better under direct vision using the hysteroscope. In this case adhesions are divided by cutting, cautery, or lysed with laser. The uterine walls are kept apart by inserting an intrauterine contraceptive device as Lippes loop which is left for three months, or better by the use of a paediatric Foley catheter which balloon is filled with 3 ml sterile saline. The catheter is left for 7 days during which a broad-spectrum antibiotic is given. The patient must be treated for 3-6 months with high doses of oestrogen, e.g. conjugated oestrogens (Premarin) 2.5 mg orally daily for 3 weeks, adding medroxyprogesterone acetate tablets (Provera) 10 mg daily during the third week. The course is repeated after one week rest. Oestrogen helps regeneration of the endometrium. Treatment leads to pregnancy in 70-80% of cases. However, the rate of abortion may be higher than normal, and the risk of placenta accreta is increased.

The Superfemale or Triple X Syndrome

The individual is a female with 47 or 48 chromosomes (47XXX or 48XXXX). The genital organs are infantile with oligomenorrhoea, amenorrhoea, infertility, and mental deficiency. Gonadotrophins may be tried to induce ovulation and menstruation but the ovaries may be refractory. However, the majority of superfemales are normal in every way and fertile.

Testicular Feminization or Complete Androgen Insensitivity Syndrome

The patient is an attractive female with well-developed large breasts with small nipples and pale areola, smooth hairless skin and normal vulva. Pubic and axillary hair are absent or scanty. The fallopian tubes and uterus are absent or rudimentary. The lower part of the vagina which is developed from the urogenital sinus is present and so the vagina is short and blind but sometimes it is of normal length. The gonads are testes and found intra-abdominally or in



Fig.25. Testicular feminization

hernial sacs in the groins or upper labia. The karyotype is 46XY (male). The target organs (breasts, hair follicles, and vulva) are not sensitive to the androgens secreted by the testes due to absence of androgen receptors and so they develop in the female direction. There is often a positive family history. It is inherited as an X-linked recessive gene. The treatment is removal of the testes to avoid malignancy (5-25%) then oestrogen is given to avoid menopausal symptoms, osteoporosis, and to maintain the feminine characteristics. If the vagina is not adequate for coitus, gradual dilatation or plastic surgery is performed. The testes are removed after puberty (at 16-18 years) and when breast development is complete. If removed before puberty the breasts will not develop because the testes are the source of oestrogen.

Notes for the postgraduate

1. Testicular feminization was first described by Morris, so also known as Morris syndrome and androgen resistant (insensitive) syndrome.
2. Testicles do not show spermatogenesis.
3. Serum testosterone is in the normal male range (7.8 nanograms/ml).
4. The Sertoli cells of the testicle produce antimüllerian hormone which inhibits the development of the müllerian duct on the same side. This explains why the fallopian tubes and uterus are absent or rudimentary.
5. Absent uterus in a normal appearing female occurs only in 2 conditions: androgen insensitivity and müllerian agenesis.
6. Incomplete androgen insensitivity syndrome. The karyotype is 46XY, female features but with some pubic and axillary hair and enlarged clitoris.

The Galactorrhoea Amenorrhoea Syndrome

See hyperprolactinaemia.

HYPERPROLACTINAEMIA

Prolactin is a polypeptide hormone secreted by lactotrophs (lactotropes) which are derived from the chromophobe cells of the anterior pituitary gland. The prolactin-inhibiting hormone or factor (PIH or PIF) which is dopamine inhibits the secretion of prolactin. Oestrogens, serotonin, and thyrotrophin releasing hormone act directly on the lactotrophs and increase prolactin secretion. The normal serum level in the female is 2-20 nanograms/ml, or 40-400 mIU/ml. The main function of prolactin is production of milk from the mammary glands, i.e., lactation. Prolactin is present in 4 forms according to its molecular weight. Small prolactin with a low molecular weight, big prolactin, big-big prolactin and glycosylated prolactin. Small prolactin is the more bioactive form of the hormone, and 80% of prolactin is present in this small form. The other 3 forms have low bioactivity and this explains the occasional presence of hyperprolactinaemia in association with normal ovulatory cycles.

CAUSES OF HYPERPROLACTINAEMIA

1. Physiological

1. Pregnancy due to high oestrogen level.
2. Lactation. Suckling and breast stimulation lead to reflex suppression of PIIH.
3. Stress. Any type of stress including exercise, vaginal examination, palpation of the breast, and difficult venous puncture when the blood sample is taken.
4. Sexual intercourse
5. Sleep. Prolactin secretion increases during sleep. The highest secretion occurs between 5 and 7 AM.
6. Frequent nipple stimulation in search for galactorrhoea in obsessed women.
7. Hypoglycaemia.

2. Pathological

1. Hypothalamic disorders leading to decreased secretion of PIIH.
 - a. Functional. There is hyperprolactinaemia in absence of a detectable cause, i.e., idiopathic hyperprolactinaemia.
 - b. Organic lesions due to trauma, infections (meningitis, encephalitis) and tumours.
 - c. Psychological disturbances as depressive psychosis.
2. Pituitary lesions: (a) Prolactin secreting tumours (prolactinomas); (b) empty sella syndrome; (c) growth hormone secreting tumour. Hyperprolactinaemia is present in about 30% of cases of acromegaly. It is due to compression of pituitary stalk by the tumour leading to deficiency of dopamine or the presence of a mixed growth hormone and prolactin secreting tumour. Pituitary adenoma is the commonest cause of hyperprolactinaemia and present in 40-50% of cases.
3. Primary hypothyroidism. The thyrotrophin releasing hormone is increased and stimulates the lactotrophs. It is responsible for 2-5% of cases.
4. Drugs. Account for 1-2% of cases and include many drugs as oestrogens, combined oral contraceptives, antihypertensives as methyl dopa (Aldomet) and reserpine, antihistaminics, antiemetics as metoclopramide (Primperan), tranquillizers, antidepressants, narcotics and phenothiazines. Drugs act by inhibiting the secretion of dopamine or block the dopamine receptors. Oestrogen directly stimulates the lactotrophs and also inhibits the secretion of dopamine.
5. Chronic liver disease. Prolactin is inactivated in the liver.
6. Chronic renal disease due to decreased excretion of prolactin.
7. Lung and renal tumours, uterine myoma, and other ectopic tumours may secrete prolactin.
8. Diseases of the chest wall as herpes zoster, diseases of the breast, mastectomy and thoracotomy. These act through inhibition of PIIH.

The commonest causes are pituitary adenoma (40-50%) and idiopathic hyperprolactinaemia.

GYNAECOLOGICAL DISORDERS ASSOCIATED WITH HYPERPROLACTINAEMIA

1. Amenorrhoea. Prolactin inhibits the pulsatile secretion of gonadotrophin releasing hormone, renders the ovary refractory to the action of pituitary gonadotrophins and inhibits ovarian steroidogenesis. About 20% of cases of secondary amenorrhoea are due to hyperprolactinaemia.
2. Oligomenorrhoea.
3. Dysfunctional uterine bleeding.
4. Anovulatory cycles. About 15% of cases of anovulation are due to hyperprolactinaemia.
5. Luteal phase defect (LPD) due to lysis of the corpus luteum (luteolysis).
6. Infertility due to anovulation and LPD.
7. Galactorrhoea. It is persistent secretion of milk or serous fluid from the breast in absence of breast-feeding. The serous fluid is clear, but may be yellow or green. It is bilateral and rarely unilateral. However, only 30-60% of women with high serum prolactin have galactorrhoea. Sometimes galactorrhoea occurs with a normal prolactin level indicating hypersensitivity of the breast tissue to the hormone. To detect galactorrhoea each quadrant of the breast should be squeezed from the periphery towards the nipple in an attempt to get a discharge. A discharge from the nipple may result from many causes, but true galactorrhoea is indicated by the presence of fat droplets demonstrated by microscopic examination or by the use of fat stains.
8. Premenstrual syndrome. Hyperprolactinaemia has been suggested as a cause.
9. Hirsutism. Prolactin increases the formation of adrenal androgens, and decreases the synthesis of sex-hormone binding globulin thus increasing free testosterone.
10. Loss of libido.
11. Severe hyperprolactinaemia (>100 ng/ml) usually leads to amenorrhoea and a hypoeostrogenic state. Oestrogen deficiency leads to osteoporosis in the long run.

DIAGNOSIS

1. History and physical examination. Exclude drugs which raise the serum prolactin.
2. Serum prolactin should be determined in the following conditions (a) amenorrhoea (primary and secondary); (b) oligomenorrhoea; (c) galactorrhoea; (d) infertility due to anovulation and luteal phase defect. A high level should be confirmed at least twice, as the level is raised by stress including attending hospital.
3. Primary hypothyroidism is excluded by measuring serum thyroid stimulating hormone (TSH) which is elevated.
4. Pituitary adenoma is excluded by computerized tomography (CT) scan of the sella turcica. Magnetic resonance imaging (MRI) is more accurate than CT scan but is costly. MRI detects all macroadenomas (more than 1 cm in diameter) and around 70% of microadenomas (less than 1 cm in diameter). A cone view of the sella turcica is done if CT scan and MRI are not available. In this case a macroadenoma will cause distortion,

expansion (ballooning) or erosion of the sella turcica. A cone view does not diagnose a microadenoma.

Notes

- Cone view means anteroposterior and lateral x-ray films of the sella turcica.
- Repeated CT scans may lead to cataract. Maximum 6 examinations in a life time are allowed.
- A prolactin level above 100 ng/ml occurs with a pituitary adenoma. However, a lower level less than 100 ng/ml may occur with a small microadenoma.
- Nanogram = millimicrogram. mIU = milli international unit.

TREATMENT

1. Treatment of the cause as primary hypothyroidism and stop the use of any causative drug.
2. Idiopathic hyperprolactinaemia is treated by dopamine agonists which include:
 - a. Bromocriptine (Parlodel). It is an ergot alkaloid. The tablet is 2.5 mg. The recommended dose is 2-3 tablets (5-7.5 mg) daily, however, larger doses may be needed (up to 6 tablets). It has ergotamine-like side effects leading to nausea, vomiting, postural hypotension, dizziness and constipation. To avoid nausea and vomiting, it must be given with meals and we start with half tablet and gradually increase by half tablet every week. The drug can be given vaginally to avoid nausea and vomiting. The drug disappears from blood after 14 hours, and so it is given 2 or 3 times daily. Bromocriptine is also available in a long-acting injection form which is given intramuscularly in a dose of 50 or 75 mg every month. The injection gives a rapid response than the oral route.
 - b. Lisuride (Dopergin). It is more potent and causes less nausea and vomiting. The tablet is 0.2 mg.
 - c. Cabergoline (Dostinex). It causes less nausea and vomiting. It is long-acting and given once weekly, and if necessary twice weekly. The tablet is 0.5 mg. The dose is 0.5-3 mg (1-6 tablets). It can also be administered vaginally for the rare patient who cannot tolerate it orally.
 - d. Quinagolide (Norprolac). A nonergot preparation and so the side effects are few. The tablets are 25, 50, and 75 micrograms. The dose is 75-300 µg once daily. Untested in pregnancy.

Serum prolactin is repeated every 6 months, and CT scan or MRI every 1-2 years as a microadenoma may appear.
3. Pituitary adenoma. Both microadenoma and macroadenoma are treated medically by a dopamine agonist as bromocriptine, which leads to shrinkage of the tumour. Treatment is continued for life, because discontinuation leads to recurrence of symptoms. However, if a microadenoma is discovered accidentally and is not producing symptoms, no treatment is given, and the woman is kept under observation. She is seen once every year to exclude appearance of symptoms, and a cone view of the sella turcica is performed. Surgical treatment is indicated in case of macroadenoma if (a) the tumour does not decrease in size with medical treatment; (b) the patient cannot tolerate the side effects of medical

treatment; and (c) when vision is affected by the tumour compressing the optic chiasma. Radiotherapy is applied for cases recurring after surgery and when the patient is unfit for surgery when indicated.

Notes for the postgraduate

- Patients who conceive in the presence of a pituitary macroadenoma should continue bromocriptine and should have the visual fields examined every trimester as the tumour may enlarge under the effect of oestrogen (risk 1% with microadenoma and 15% with macroadenoma). The drug is not teratogenic.
- In the past when estimation of serum prolactin was not possible three syndromes were described. The Chiari-Frommel syndrome was applied to amenorrhoea-galactorrhoea following delivery. Ahmada-Del-Castillo syndrome was applied to amenorrhoea-galactorrhoea in the nullipara. Forbes-Albright syndrome indicating the same disorder in a patient with pituitary adenoma. These syndromes are of historic interest and are due to hyperprolactinaemia due to any cause which leads to amenorrhoea and galactorrhoea.
- No harm results from breast feeding, if the patient is having a pituitary adenoma.
- Hyperprolactinaemic women can use low-dose combined oral contraceptives for birth control. The low-oestrogen dose will not increase prolactin secretion, and will not increase the growth of a pituitary microadenoma.
- The success rate of treatment of anovulation due to hyperprolactinaemia is very high (about 90%), and the response is rapid.
- Bromocriptine stimulates dopamine D_2 -receptors leading to inhibition of prolactin secretion. The side effects are mainly due to stimulation of dopamine D_1 -receptors, serotonin, and α_1 -adrenergic receptors. Norprolac stimulates only D_2 -receptors and so side effects are few.
- Galactorrhoea is investigated in every woman. However, in a lactating woman, investigation is carried out one year after weaning.

ABNORMAL UTERINE BLEEDING

This includes polymenorrhoea, menorrhagia, metrorrhagia, menometrorrhagia and intermenstrual bleeding.

POLYMENORRHOEA

It is frequent menstruation. The menstrual cycle is less than 21 days.

Aetiology

Polymenorrhoea is due to a short proliferative or a short secretory phase. The short proliferative phase results from early maturation of the graafian follicle which may result from pituitary hyperstimulation. The short secretory phase is due to early degeneration of the corpus luteum, and is the result of:

1. Ovarian congestion as a part of pelvic congestion as in case of fibroids, retroversion, chronic pelvic infection, etc.
2. Hypothyroidism.



3. Dysfunctional polymenorrhoea occurring shortly after menarche, near the menopause, after abortion or labour. The early degeneration of the corpus luteum occurs in the absence of an organic cause.

Treatment

1. Progestogens given in the second half of the cycle, as norethisterone (Primolut-N tablets) 10 mg daily for 10 days starting on day 15 of the cycle.
2. A combined oral contraceptive is given for 21 days each month.
Hormonal treatment is given for 3 successive months to prevent recurrence of abnormal bleeding.
3. Thyroxine if there is hypothyroidism.
4. Treatment of anaemia if present.

MENORRHAGIA

It is excessive and/or prolonged menstruation. Menstruation is excessive if the amount of menstrual blood is greater than 80 ml. Menstruation is prolonged if bleeding continues for more than 7 days.

Aetiology

A. General Causes

(1) Hypertension; (2) congestive heart failure; (3) blood diseases as leukemia, thrombocytopenia, and von Willebrand disease; (4) hypo- and hyperthyroidism; (5) anticoagulant therapy; (6) liver disease particularly cirrhosis (may impair metabolism and excretion of oestrogen leading to hyperoestrinism, endometrial hyperplasia and menorrhagia. Also clotting factors may be affected with cirrhosis. There is also decreased synthesis of sex-hormone binding globulin leading to increased free oestrogen); (7) psychological disturbances (acting through the hypothalamus or through the autonomic nervous system affecting uterine blood vessels leading to pelvic congestion); (8) smoking leading to anovulation and unopposed oestrogen effect.

Note. Hypertension leads to menorrhagia when it is associated with atherosclerosis of the uterine vessels.

B. Local Causes

All causes of pelvic congestion:

(1) chronic pelvic infection as salpingitis; (2) pelvic tumours; (3) abnormal position of uterus as retroversion or prolapse; (4) simple pelvic congestion as in chronic constipation; (5) pelvic congestion syndrome due to broad ligament varicocele; (6) endometriosis and adenomyosis; (7) extragenital causes as chronic appendicitis.

Also menorrhagia is a common complication of intrauterine contraceptive devices and may complicate tubal sterilization. The abnormal uterine bleeding which may follow tubal

sterilization is explained by interference with ovarian blood supply leading to luteal phase defect or it is due to the effect of aging as the procedure is often done after the age of 35. Menorrhagia may also occur with a bicornuate uterus, due to increased surface area of the endometrium.

C. Dysfunctional Menorrhagia

Bleeding occurring in absence of an organic cause. It is due to irregular ripening or irregular shedding of the endometrium. In case of irregular ripening there is poor function of the corpus luteum so the endometrium is without enough hormonal support and bleeding starts several days before menstruation. Premenstrual endometrial biopsy will show mixed proliferative and secretory changes. In case of irregular shedding, there is slow and incomplete degeneration of the corpus luteum, so bleeding continues for several days after the proper flow. When the endometrium is examined on the 4th or 5th day of menstruation, it will show areas of secretory changes while the endometrium should be in the early proliferative phase. Sometimes we have anovulatory menorrhagia.

Treatment

1. General treatment. Rest in bed. Blood transfusion may be needed in severe cases. Correction of anaemia.
2. Treatment of the cause as hypertension.
3. Non-hormonal treatment:
 - a. Antifibrinolytic agents can be given because the fibrinolytic activity in the endometrium is increased in case of menorrhagia. They reduce the menstrual blood loss by 50% in most of the cases. Tranexamic acid (Cyklokapron tablets, 500 mg) is given as 1 g (2 tablets) orally 2-4 times daily during the period. Contraindicated if there is a previous history of thromboembolic disease.
 - b. Antiprostaglandins as ibuprofen (Brufen tablets, 400 mg three times daily during the period). The menstrual blood loss is reduced by about 25%. In case of menorrhagia, there is increased production of prostaglandin (PG) E_2 and prostacyclin (PGI₂). PGE₂ is a vasodilator and prostacyclin causes vasodilatation and prevents aggregation of platelets which is necessary for thrombus formation.
 - c. Haemostatic agents as diosmin (Daflon) and ethamsylate (Dicynone) tablets. The tablet is 500 mg. Two tablets are given twice daily during the bleeding. The drugs act by decreasing capillary fragility and increasing aggregation of platelets.
4. Hormonal treatment:
 - a. Progestogens as norethisterone (Primolut-N) tablets. The tablet is 5 mg. The dose is 10-15 mg (2-3 tablets) daily for 20 days. When treatment is stopped shedding of the endometrium and withdrawal bleeding occurs, i.e., medical curettage. Progestogens are of value in cases of anovulatory bleeding (absent progesterone) and luteal phase defect (inadequate production of progesterone). Medroxyprogesterone acetate

(Provera) tablets can also be used (it is non-androgenic). To prevent recurrence of bleeding we give 10 mg daily for 10 days in the second half of the cycle every month for at least 3 successive months.

- b. Combined oral contraceptives. One tablet is given 2 or 4 times daily until the bleeding stops, then one tablet daily for 20 days. They act by creating atrophic endometrium. The tablets are then given in the usual way for at least 3 successive months.
 - c. Danazol. It is a weak synthetic androgen. The dose is 200 to 400 mg daily and continuously for 3 months. The 200 mg daily reduce the menstrual blood loss by 50%, while the 400 mg daily usually lead to amenorrhoea. The drug is very expensive and has many side effects, however, it can be used when the combined oral contraceptives and progestogens are contraindicated, or ineffective (intractable menorrhagia).
 - d. Gestrinone. It is a weak synthetic androgen which acts like danazol and has the same side effects. The dose is 1.25-2.5 mg given twice weekly for 3 months.
 - e. Thyroxine is given if there is hypothyroidism.
 - f. Gonadotrophin releasing hormone analogues (agonists). They lead to amenorrhoea. They are given as daily nasal spray, or intramuscular or subcutaneous injections every 4 weeks for 3 successive months. They can be used for intractable menorrhagia.
 - g. Induction of ovulation with clomiphene citrate (Clomid). This may help in case of anovulatory bleeding. However, it is used only if the patient desires pregnancy.
 - h. Progesterone or levonorgestrel releasing intrauterine device (Mirena IUD). It can be applied to reduce blood loss particularly in cases of chronic renal failure, blood dyscrasias, kidney and liver transplant to avoid the metabolic and systemic side effects of sex hormones. Mirena device reduces menstrual blood loss by more than 80%.
5. Surgical treatment:
- a. Uterine curettage. Indications: (a) If the bleeding is severe; (b) if it fails to respond to other lines of treatment; (c) if the patient is above 40 to exclude endometrial carcinoma. The advantages are (a) it arrests bleeding in about 60% of cases by removing the necrotic endometrium, (b) it determines the type of dysfunctional bleeding, (c) may reveal an organic cause as endometrial carcinoma.
 - b. Hysterectomy. Indicated when all lines of treatment fail including repeated curettage at least twice.
 - c. Endometrial ablation. It is performed when hysterectomy is refused and when the patient is unfit for hysterectomy as in case of marked obesity, severe hypertension, or diabetes mellitus. The endometrium is destroyed by laser, thermal ablation, as well as other methods.

METRRORRHAGIA

It is irregular uterine bleeding not related to menstruation. The causes are: (1) local lesion in the genital tract which may be traumatic, inflammatory or neoplastic; (2) complications of pregnancy as abortion and hydatidiform mole; (3) irregular intake of hormones or

contraceptive tablets; (4) the presence of intrauterine device; (5) dysfunctional metrorrhagia as in metropathia haemorrhagica and threshold bleeding.

MENOMETRORRHAGIA

It is menorrhagia associated with irregular intermenstrual bleeding.

INTERMENSTRUAL BLEEDING

It is bleeding that occurs between normal menstrual cycles.

Note for the postgraduate

Thyroid disorders lead to abnormal uterine bleeding by several mechanisms: (1) hyperthyroidism leads to rapid excretion of oestrogens in urine; (2) thyroxine may have a direct effect on the spiral arterioles of the endometrium, and on haemostasis during menstruation; (3) hyperthyroidism increases the liver synthesis of sex-hormone binding globulin (SHBG) and thus decreases free serum oestradiol (hypoestrogenic state). Hyperthyroidism commonly leads to amenorrhoea and oligomenorrhoea, but can also lead to menorrhagia. Hypothyroidism decreases the SHBG and increases free serum oestradiol. Hypothyroidism commonly leads to menorrhagia, but can also lead to amenorrhoea and oligomenorrhoea. Primary hypothyroidism may cause hyperprolactinaemia which can lead to amenorrhoea.

METROPATHIA HAEMORRHAGICA (SCHROEDER DISEASE)

Aetiology

The exact cause is unknown. The graafian follicle fails to rupture, and continues to grow to form a cyst. Large amounts of oestrogen are produced which act on the uterus. When oestrogen reaches a high level it inhibits the secretion of FSH of the anterior pituitary and this is followed by degeneration of the cystic follicle and drop in the level of oestrogen resulting in separation of the endometrium and withdrawal bleeding, or the endometrium grows so thick that its blood supply becomes inadequate leading to necrosis and sloughing.

Pathology

1. The Uterus

It is slightly symmetrically enlarged and soft in consistency due to increased vascularity. There is hypertrophy of the myometrium. The endometrium is thickened, haemorrhagic and may become polypoidal. Microscopically, the endometrium shows simple hyperplasia (cystic glandular hyperplasia): (a) the glands are increased in number and become cystic and lined by cuboidal or columnar epithelium; (b) there is variation in the size of the glands giving a "Swiss cheese" appearance; (c) no evidence of secretory changes; (d) the stroma is dense and oedematous; (e) areas of necrosis and haemorrhage may be seen.

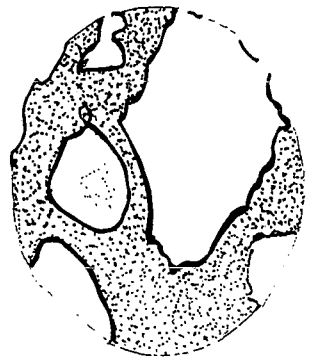


Fig.26. Cystic hyperplasia of the endometrium

2. The Ovaries

One ovary is enlarged and cystic. It contains one or multiple follicular cysts lined by granulosa cells. A corpus luteum is absent. The cysts may be bilateral. The cysts are less than 5 cm in diameter, i.e., functional cysts.

Note. Cystic glandular hyperplasia is an old term and has been replaced by simple endometrial hyperplasia.

Diagnosis

Age Incidence

The condition is more common near the menopause or shortly after menarche.

Symptoms

There is severe painless uterine bleeding unrelated to menstruation. It may continue for several days or weeks. In about 50% of cases the bleeding is preceded by a short period of amenorrhoea lasting 6-8 weeks. In other cases it is preceded by menorrhagia or normal menstruation. Symptoms of anaemia may be present. Bleeding is painless because it is anovulatory.

Signs

The uterus is slightly symmetrically enlarged and soft. One or both ovaries may be felt enlarged and cystic.

Investigations

1. Ultrasonography shows enlarged uterus, thick myometrium, thick endometrium, and follicular cysts in one or both ovaries. The cysts are less than 5 cm in diameter.
2. Endometrial biopsy confirms the diagnosis by showing the picture of simple endometrial hyperplasia.

Differential Diagnosis

Causes of uterine bleeding associated with symmetrically enlarged uterus as abortion, ectopic pregnancy and submucous fibroid.

Treatment

The same lines of treatment mentioned with menorrhagia.

THRESHOLD BLEEDING

In this case the endometrium is thin with a poorly developed proliferative phase. The ovary is producing small amounts of oestrogen which reach the threshold for bleeding but not enough to produce a full proliferative phase. The suggested oestrogen level which causes bleeding is a serum level between 50 and 100 picograms/ml. A level below 50 or above 100 pg/ml is associated with amenorrhoea. The clinical picture is like metropathia haemorrhagia

and differentiated only by uterine sonography and curettage. Treated by oestrogen given for 21 days with a progestogen added during the last week of therapy. Treatment is repeated for 3 months.

Note. Metropathia haemorrhagia = irregular uterine bleeding + too much oestrogen and no progesterone. Threshold bleeding = irregular uterine bleeding + too little oestrogen and no progesterone.

DYSFUNCTIONAL UTERINE BLEEDING (DUB)

Definition

It is abnormal uterine bleeding occurring in the absence of any systemic or organic cause in the genital tract. The dysfunction may arise in the endometrium, ovary, pituitary, hypothalamus or higher centres.

Notes

- The endometrial dysfunction is related to excessive production of prostaglandin E_2 and prostacyclin or increased fibrinolytic activity of the endometrium. PGE_2 causes vasodilatation and relaxation of the nonpregnant uterus (but contraction of the pregnant uterus). Prostacyclin (PGI_2) causes vasodilatation and inhibits platelet aggregation.
- Systemic causes as thyroid dysfunction and bleeding disorders.

Age incidence

It is more common near the menopause (50% of the cases), or shortly after menarche (20% of the cases). More common near menopause due to decreased number of ovarian follicles and their increased resistance to gonadotrophin stimulation. More common shortly after menarche due to immaturity of the hypothalamic-pituitary-ovarian axis.

Classification

Clinically, the bleeding may be cyclic in the form of menorrhagia or polymenorrhoea, or it may be acyclic as in case of metropathia haemorrhagica and threshold bleeding. According to the histological picture of the endometrium, the bleeding may be ovulatory when the endometrium shows secretory changes or anovulatory in absence of the latter. Metropathia haemorrhagica and threshold bleeding are examples of anovulatory bleeding.

Endometrial Histology in DUB

The endometrium may be proliferative, hyperplastic, atrophic, secretory or mixed which is partly proliferative and partly secretory.

Diagnosis

A. History

Personal history

1. Age of the patient, dysfunctional bleeding is more common near the menopause or shortly after menarche.
2. Marital state to exclude complications of pregnancy as abortion.

Present history

Ask about the amount, character, and duration of bleeding, its type whether cyclic or acyclic. The presence of other symptoms as pain and foul discharge, urinary and gastrointestinal symptoms.

Past history

1. Diseases as hypertension, heart failure, haemorrhagic blood diseases as leukemia, and inherited bleeding disorders as von Willebrand disease.
2. Contraceptive tablets intake.

Menstrual history

If bleeding is preceded by a short period of amenorrhoea suspect pregnancy or metropathia haemorrhagica.

Obstetric history

A recent abortion, labour, or passage of a hydatidiform mole may direct attention to choriocarcinoma.

B. General Examination

For signs of anaemia, signs of bleeding disorders in the form of bruising and petechiae, presence of cachexia, and the presence of a general cause as hypertension or thyroid disease.

C. Abdominal Examination

For a pelvi-abdominal mass as fibroid or pregnancy.

D. Pelvic Examination

To detect a local cause for the bleeding. The urethra and anal canal are excluded as a source of bleeding as urethral caruncle or piles. If no general or local cause is found to explain bleeding, it is provisionally diagnosed as dysfunctional. However, further investigations may show an organic cause.

E. Special Investigations

1. Transvaginal sonography. It excludes the presence of an ovarian tumour or a lesion in the uterus as fibroids or endometrial carcinoma.
2. Cervical smear. Taken in absence of bleeding to detect the presence of malignant cells which may come from the cervix, endometrium, tubes, or ovaries.
3. Endometrial biopsy. This must be done in every woman above the age of 40 years complaining of abnormal uterine bleeding, as it is the only sure method to exclude endometrial carcinoma. Endometrial biopsy is taken by one of three methods; fractional uterine curettage, endometrial aspiration (using Pipelle suction curette or Vabra aspirator), or hysteroscopy.

4. Laboratory tests. These are done according to the clinical findings and include:
 - a. Complete blood count.
 - b. Platelet count, bleeding time, coagulation time, estimation of clotting factors if a bleeding disorder is suspected from the history or clinical examination.
 - c. Thyroid function tests if we suspect a thyroid disorder.
 - d. Liver function tests if we suspect a liver disease.
 - e. Serum progesterone done on day 22-24 to diagnose luteal phase defect and anovulation.
5. Laparoscopy. It is indicated when treatment fails to control bleeding. It may reveal an organic cause in the pelvis as a small oestrogenic ovarian tumour.

Treatment

- Treatment of polymenorrhoea: See page 72.
- Treatment of menorrhagia and metrorrhagia: See page 73.
- Treatment of threshold bleeding. See page 76.

POSTMENOPAUSAL BLEEDING

It is bleeding from the genital tract occurring 6 months or 1 year by some gynaecologists or more after menopause. It is a serious symptom because in about 25% of cases, it is due to a malignant lesion in the genital tract.

Prevalence

About 7 per 1000 postmenopausal women.

Aetiology

(A) General Causes

(1) Oestrogen therapy (25%). Oestrogen given for menopausal symptoms may lead to withdrawal bleeding; (2) blood diseases as leukemia; (3) anticoagulant therapy; (4) Ginseng is obtained from the root of some plants, and is included in some tonics and antioxidants. It has a weak oestrogenic effect and may cause bleeding.

(B) Local Causes

1. **Vulva.** Malignant tumour, fissured leucoplakia, urethral caruncle, and direct trauma.
2. **Vagina.** Malignant tumour, senile vaginitis, trophic ulcer in prolapse, and retained foreign body or pessary in the vagina.
3. **Cervix.** Malignant tumour, erosion and ulcers.
4. **Uterus.** Malignant tumour, senile endometritis, tuberculous endometritis, fibroid undergoing malignant change or a fibroid polyp showing necrosis at its tip or endometrial hyperplasia resulting from unopposed oestrogen action, the source of which is an oestrogenic ovarian or adrenal tumour or peripheral conversion of

androgens to oestrogens mainly occurring in body fat as in case of obese women who are liable to develop endometrial carcinoma.

5. **Tube. Carcinoma.** This leads to a watery vaginal discharge which finally becomes blood stained.
6. **Ovary. Carcinoma** with metastases in the endometrium and oestrogenic ovarian tumours.

(C) In about 15% of cases no cause is found after physical examination and uterine curettage which shows atrophic endometrium.

Diagnosis

A. History

Personal history

(a) Age: The commonest age incidence for carcinoma of uterus is 55-70 years while that for carcinoma of the vulva is 60-70 years; (b) parity: some tumours are more common among nulliparae e.g. endometrial and ovarian carcinoma.

Present history

Ask about the amount, character and duration of bleeding, duration of menopause, and the presence of other symptoms as pain and foul discharge, urinary and gastrointestinal symptoms (malignant invasion of bladder or bowel).

Past history

(a) Oestrogen therapy; (b) diseases as diabetes mellitus, hypertension and blood diseases as leukemia. Endometrial carcinoma is more common in diabetic hypertensive patients.

Family history

Carcinoma of the body of the uterus and ovary have a familial tendency.

B. General Examination

(1) Signs of anaemia; (2) signs of bleeding disorders; (3) presence of cachexia; (4) examination of heart and chest for secondaries; (5) estimation of blood pressure.

C. Abdominal Examination

For a pelvi-abdominal mass and ascites which is common with ovarian malignancy.

D. Pelvic Examination

To detect a local cause for bleeding. The urethra and anal canal are excluded as being the source of bleeding as urethral caruncle or piles.

E. Special Investigations

1. Transvaginal sonography. It excludes the presence of an ovarian tumour or a lesion in the uterus as endometrial carcinoma.

SIXTH EDITION

BASIC GYNAECOLOGY

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To ...

Mai, Alaa

and Nevine

First Edition 1976

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Fourth Edition 1997

Fifth Edition 2001

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Sixth Edition 2007

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PREFACE

This book was first published in 1975. It is thus the longest-standing textbook in Gynaecology published in Egypt. Basic Gynaecology has moved into its sixth edition, but the mission has remained the same -- to provide basic and current information on a broad range of topics for students, residents, and practising physicians.

All the chapters have been revised and updated. However, with the passage of even a few years, new knowledge will supersede. As usual, I have learned a great deal from preparing this edition, and still teaching others continues to be a great joy to me.

I would like to express my gratitude to Professor Abdel Karim El-Hemaly and Professor Ibrahim Mahrous for providing me with their new concepts in the aetiology, ultrasonographic findings, and surgical treatment of genuine stress incontinence. I am indebted to the publisher Mr. Sayed Mahmoud for his untiring and effective help. I must acknowledge Doctor Essam Hoballah for his invaluable assistance in typing the manuscript. I also thank Mr. Sayed Abd El-Naby for preparing the illustrations.

Farouk Haseeb

Cairo, 2007

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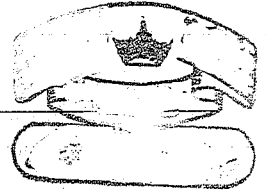
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SECTION I

ANATOMY, EMBRYOLOGY AND PHYSIOLOGY



ANATOMY

THE EXTERNAL GENITAL ORGANS

The vulva means the external genitalia and is composed of the following structures:

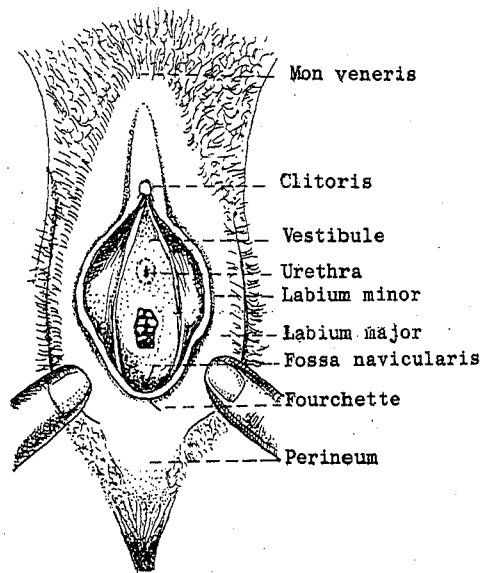


Fig.1. Vulva

1. Mons Pubis or Veneris

It is a mass of fat covered by skin and hair and overlies the symphysis pubis. The pubic hair may be feminine with an upper straight border or masculine with a convex upper border.

2. Labia Majora

Two folds of skin on either side of the vaginal orifice. Anteriorly they unite with the mons veneris, posteriorly they join each other to form the posterior commissure and unite with the skin of the perineum. Each labium major contains a mass of fat and the skin is covered with hair and contains sebaceous and sweat glands. Some of the sweat glands are large and coiled and known as apocrine glands; and their secretion gives rise to a characteristic odour. The apocrine gland produces a secretion which contains secretory cells of the gland itself.

3. Labia Minora (nymphae)

Two thin flaps of nonkeratinized pigmented skin lying within the labia majora on either side of the vaginal orifice. Anteriorly, each labium minor divides into 2 flaps, the upper flaps unite above the clitoris to form the prepuce, while the lower flaps join to form the frenulum of the clitoris. The labia minora unite posteriorly to form a sharp fold of skin called the fourchette. The depression between the fourchette and the hymen is the fossa navicularis. The labium minor contains loose connective tissue devoid of fat and is very vascular so it becomes turgid during sexual excitement. The skin contains many sebaceous glands but no sweat glands or hair follicles.

4. Clitoris

It is the homologue of the penis, lies in front of the symphysis pubis and attached to it by a suspensory ligament. It is 1-2 cm in length and made of glans, prepuce, body and two crura attached to the pubic arches. It consists of erectile tissue and is the most sensitive part of the vulva as it is richly supplied with nerves.

5. Vestibule

It is a triangular area lying within the labia minora with the clitoris at its apex. The external urethral meatus, the vaginal orifice and Bartholin glands open at the floor of the vestibule.

6. The External Urethral Meatus

Present in the anterior part of the vestibule. The Skene tubules are two paraurethral ducts which open in the floor of the urethra 1 cm from the external meatus (4-6 mm in diameter). The Skene tubules are homologous to the prostate in the male. The length of female urethra in the adult is 3-4 cm. Its proximal two-thirds are lined by transitional epithelium and distal third is lined by stratified squamous epithelium.

7. Hymen

A fold of mucous membrane at the vaginal orifice. It consists of fibrous tissue and is covered on both sides by stratified squamous epithelium. It has one or more openings to allow escape of menstrual blood. It may be annular, crescentic, biperforate, cribriform or imperforate. The hymen is torn as a result of sexual intercourse unless it is abnormally elastic. The bleeding is usually slight as the hymen contains few blood vessels. During delivery the hymen becomes destroyed leaving small tags or nodules of fibrous tissue around the vaginal orifice called carunculae myrtiformes or hymenalis.

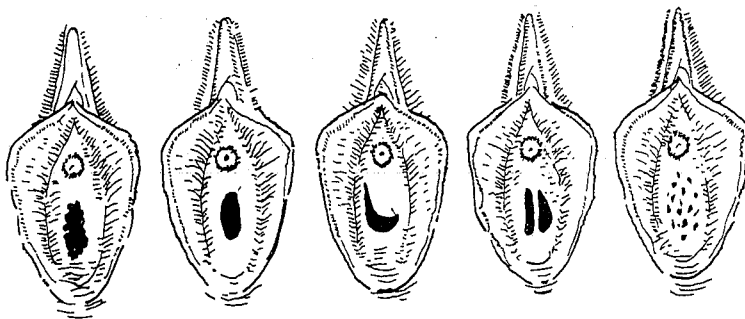


Fig.2. The different shapes of the hymen

8. Vestibular Bulbs

These are two collections of erectile tissue surrounding the vaginal orifice deep to the bulbocavernosus muscles (vaginal sphincter).

9. Bartholin Glands

Two in number. The gland lies embedded in the posterior part of the vestibular bulb, one on either side. The gland is oval and the size of a pea (1 cm in diameter), it has a duct one inch in length which passes medially to open in the floor of the vestibule lateral to the hymen at the 5 and 7 o'clock positions. Normally, the gland is not felt unless diseased and the opening of the duct is not seen. It is a compound racemose gland, the acini are lined by a single layer of columnar epithelium and the duct is lined by transitional epithelium. In response to sexual excitement the gland produces a mucoid colourless secretion to act as a lubricant for coitus. The glands are homologous to Cowper glands in the male.

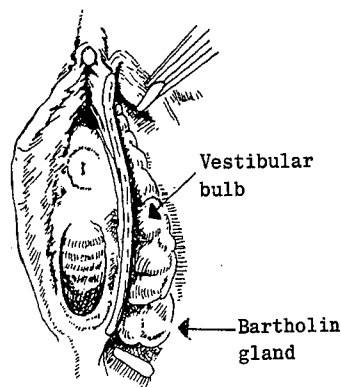


Fig.3. Bartholin gland

BLOOD SUPPLY OF THE VULVA

Branches from the internal and external pudendal arteries. The veins accompany the corresponding arteries, but those from the clitoris join the vaginal and vesical plexuses of veins.

LYMPHATIC DRAINAGE

Inguinal and femoral lymph nodes on both sides because there is crossing of lymphatics. These drain in the lymph node of Cloquet or Rosenmuller present in femoral canal → external iliac glands → common iliac glands → aortic glands.

NERVE SUPPLY

The pudendal nerve supplies motor and sensory fibres to the vulva and perineum. The ilioinguinal, genital branch of genitofemoral and posterior cutaneous nerve of the thigh also give sensory supply to the vulva.

Note for the postgraduate: Distribution of the lymph nodes which drain the vulva:

1. Superficial inguinal nodes. Lateral group which lies below the inguinal ligament, and medial group lying below the external inguinal ring.
2. Deep inguinal nodes. When present the glands lie in the inguinal canal.
3. Superficial femoral nodes. Lateral and medial groups on either side of the great saphenous vein as it enters the femoral vein at the fossa ovalis.
4. Deep femoral nodes. Lie in the femoral canal and usually represented by a single node; the node of Cloquet or Rosenmuller.
5. External iliac nodes. A group medial to the external iliac vein, a group lateral to the external iliac artery, and a third group -- if present -- in the sulcus between artery and vein.

INTERNAL GENITAL ORGANS

THE VAGINA

Anatomy

It is an elastic fibromuscular tube. It is directed upwards and backwards forming an angle of 60 degrees with the horizon. The upper end is blind and called the vaginal vault. The cervix pierces the upper part of the anterior vaginal wall and divides the vaginal vault into four areas; the anterior fornix in front of the cervix, the posterior fornix which is deep and wide and two lateral fornices. The anterior vaginal wall is about 3 inches in length and the posterior wall is 4 inches in length.

Relations

Anterior wall. It is related to the urinary bladder, urethra, and skene tubules which open into the urethra.

Posterior wall. Its upper third is related to the peritoneum of Douglas pouch, its middle third to the ampulla of the rectum, and its lower third is related to the perineal body.

Lateral wall. Related to the following structures from above downward: cardinal ligament, pelvic connective tissue, levator ani muscle, urogenital diaphragm (triangular ligament) with its attached muscles, vestibular bulb, bulbocavernosus muscle, and Bartholin gland. The ureter lies about 2 cm above the lateral vaginal fornix and 2 cm lateral to the cervix. The uterine artery crosses over the ureter at this point.

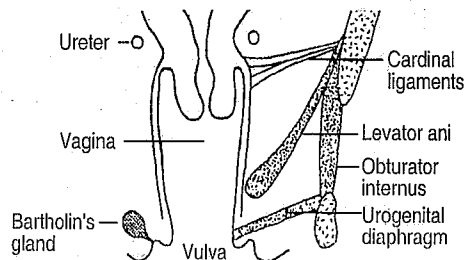


Fig. 3-2. Lateral relations of the vagina.

Structure

1. **Vaginal Mucosa.** It is thrown into transverse folds or rugae which allow the vagina to distend. It is lined by stratified squamous epithelium which contains glycogen. Glycogen is broken down into lactic acid by Döderlein bacilli, so the reaction of the vagina is acidic, the pH is 3.5-4.5 (around 4). The mucosa does not contain glands but the vagina is kept moist by a serous transudate from its wall. Oestrogen stimulates the deposition of glycogen into the vaginal mucosa.
2. **Submucosa.** It is a layer of connective tissue which contains elastic fibres.
3. **Muscle layer.** Made of outer longitudinal and inner circular smooth muscle fibres.
4. Outside the muscle layer there is a sheath of connective tissue.

Blood Supply

Vaginal artery and branches of uterine, internal pudendal, middle and inferior rectal arteries.

Lymphatic Drainage

The upper two-thirds of the vagina drain with the cervix, and the lower third drains with the vulva.

Nerve Supply

Upper two-thirds like the uterus and the lower third receives nerve supply from the pudendal nerve.

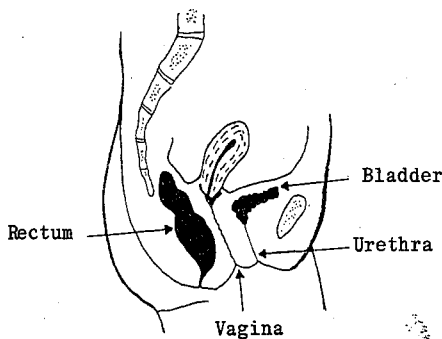


Fig.4. Relations of the vagina

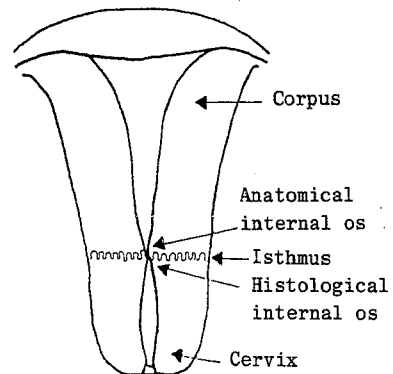


Fig.5. uterus

THE UTERUS

Anatomy

The uterus is a hollow pear-shaped muscular organ. In the nullipara the uterus is 1 inch in thickness, 2 inches across its widest part and 3 inches in length (1 x 2 x 3). In the multipara it is 1.5 x 2.5 x 3.5 inches. The weight is about 40-50 g in the nullipara and 70-80 g in the multipara.

Body

Two or two and half inches in length. The area of insertion of the fallopian tube is called the cornu. The part of the body above the insertion of the fallopian tubes is called the fundus.

Cervix

One inch in length, has a spindle shaped canal which communicates above with the uterine cavity at the anatomical internal os and below with the vagina at the external os. Half of the cervix projects into the vagina (portio vaginalis) and half is above the attachment of the vagina (supravaginal part).

Isthmus

It is a narrow part 1/2-1 cm in length below the anatomical internal os of the cervix. It is the area between the anatomical internal os and histological internal os which is at the junction of uterine mucosa and cervical mucosa (seen microscopically). Progesterone causes contraction and oestrogen causes relaxation of the isthmus. It is lined by modified endometrium with few short glands. During pregnancy the isthmus and lower part of the body of the uterus covered by loose peritoneum form the lower uterine segment.

Relations

The uterus is related anteriorly to the urinary bladder and uterovesical pouch. Posteriorly to Douglas pouch and loops of intestine. Laterally to the contents of the broad ligament including the ureter which lies 2 cm lateral to the cervix (supravaginal part).

Structure of The Body

1. Endometrium or mucous membrane, made of simple tubular glands embedded in a connective tissue stroma. It is lined by columnar ciliated epithelium but the cells lining the glands are non ciliated. The thickness of endometrium varies between 1-8 mm according to the phase of menstrual cycle.
2. Myometrium. Half inch in thickness, its plain muscle fibres are arranged into three layers: outer longitudinal, inner circular and middle interlacing fibres forming figures of 8 around the blood vessels to control bleeding (living ligatures).
3. Peritoneal coat or perimetrium.

Structure of The Cervix

It consists of collagenous connective tissue and smooth muscle fibres (15%). The mucous membrane lining the cervical canal is covered by tall columnar epithelium. Beneath which is a layer of cubical (reserve or basal) cells from which new surface cells develop. The mucosa of cervical canal contains grooves and crypts often referred to as compound racemose glands. The cells lining these crypts secrete mucus. The portio vaginalis is covered by stratified squamous epithelium. The cervical mucus is alkaline (pH 8.5), contains proteins and fructose for nutrition of spermatozoa. It has bactericidal properties to prevent ascent of infection. The

mucous membrane of the endocervical canal of the nullipara is arranged in longitudinal folds, the plicae palmatae, with secondary transverse branching folds, the arbor vitae. These folds disappear following vaginal delivery.

Blood Supply of Uterus

(1) Uterine arteries; (2) branches of ovarian arteries. The uterine artery arises from the anterior branch of the internal iliac artery. The ovarian arteries arise from the aorta.

Lymphatic Drainage. See cervical and endometrial carcinoma.

Nerve Supply

The uterus, cervix, and upper two-thirds of the vagina are supplied by the autonomic nervous system which has both sympathetic and parasympathetic fibres. The sympathetic fibres are derived from the presacral nerve or plexus of nerves which lies in front of the 4th and 5th lumbar vertebrae and sacral promontory. The parasympathetic fibres are derived from the 2nd, 3rd, and 4th sacral nerves. The sympathetic fibres produce muscular relaxation and vasoconstriction, and the parasympathetic fibres produce the opposite effects. The motor sympathetic fibres are derived from T-5, and T-6. Sensory fibres from the body of the uterus accompany the sympathetic nerves which enter the spinal segments T-10, T-11, T-12, and L-1. Sensory fibres from the cervix accompany the 2nd, 3rd, and 4th sacral nerves.

Note. The uterus is sensitive to distension and the cervix is sensitive to dilatation. Both are insensitive to burning, cutting, touch or freezing.

Ligaments Attached to The Body of Uterus

1. The Round Ligaments

Two fibromuscular cords, each is attached to the cornu of uterus and runs laterally via the broad ligament to reach the internal abdominal ring then passes through the inguinal canal to become inserted in the upper part of the labium major in a fanlike fashion. The ligament is supplied by 2 arteries, one branch from ovarian artery (Sampson artery) and one branch from inferior epigastric artery. The round ligaments seem to prevent backward displacement of the uterus. The thickness of the ligament is 5-6 mm, but undergoes marked hypertrophy during pregnancy.

2. Ovarian Ligaments

Two fibromuscular cords, each connects the lower pole of the ovary to the cornu of uterus.

3. Broad Ligaments

Each is a fold of peritoneum running from the side of the uterus to the lateral pelvic wall. Its upper outer part is called the infundibulopelvic ligament which attaches the upper pole of ovary and infundibulum of the tube to the pelvic wall. The broad ligament contains the fallopian tube, the round ligament, the ovarian ligament, the mesovarium, the mesosalpinx,

embryonic remnants of the Wolffian system, the ureter, blood vessels (uterine and ovarian) lymphatics, nerves (sympathetic and parasympathetic) and pelvic connective tissue called parametrium. The ureter passes in the base of the broad ligament.

Cervical Ligaments

These are made of condensed pelvic connective tissue, smooth muscle fibres and elastic tissue. There are 3 pairs of ligaments:

a. The Transverse Cervical Ligaments (*Mackenrodt or Cardinal ligaments*)

Each ligament extends from the lateral side of the supravaginal cervix and vaginal vault and passes laterally in a fan-shaped manner to be inserted in the white line at the lateral pelvic wall. The ureter passes through the ligament in the ureteric canal. The cardinal ligaments form the base of the broad ligaments. The white line is a thickened line in the obturator fascia, which covers the obturator internus muscle.

b. Uterosacral Ligaments

Extend from the supravaginal cervix and vaginal vault and pass backwards surrounding the rectum to be inserted partly in the rectum and partly in the third piece of sacrum.

c. Pubocervical Ligaments

Extend from the supravaginal cervix and vaginal vault and pass forwards beneath the bladder and surrounding the upper part of the urethra to be inserted in the back of the symphysis pubis.

The cervical ligaments are responsible for keeping the uterus at its normal position.

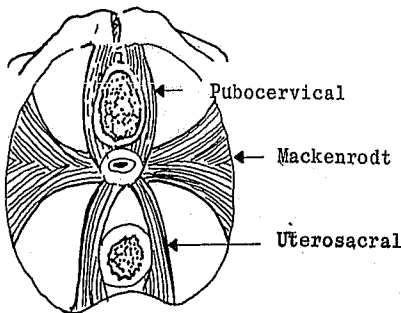


Fig.6. Cervical ligaments

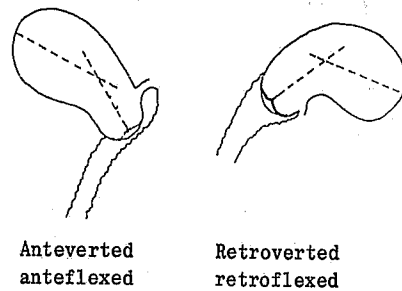


Fig.7. Position of uterus

Position of The Uterus

With the bladder empty, the uterus occupies a central position in the pelvis, with the external os at the level of the ischial spines. Normally, the uterus is anteverted anteflexed. Anteverted means the cervix is bent forwards on the vagina forming an angle of about 90 degrees. Anteflexed means the body of the uterus is bent forwards on the cervix forming an angle of about 160 degrees. In about 15% of normal women, the uterus is retroverted or

retroflexed or both, i.e. retroversion-flexion, or RVF. Retroverted means the cervix is bent backwards on the vagina, so that the external os points downwards and forwards or even directly forwards. Retroflexed means the body is bent backwards on the cervix.

Notes

- Anteversion is caused by development of tone in the uterosacral ligaments and helped by the weight of abdominal organs. Anteflexion is due to more growth of the posterior than of the anterior wall of the uterus.
- Cochleate uterus. The cervix is retroverted and the body of uterus is acutely anteflexed on the cervix, and so the uterus becomes C-shaped like the cochlea in the ear.

THE FALLOPIAN TUBES

Anatomy

The tube extends from the cornu of the uterus to the ovary. It runs in the upper free border of the broad ligament, about 10 cm in length (8-14 cm). It is divided into 4 parts:

1. The interstitial portion, which runs in the uterine wall, about 1-2 cm in length and 1 mm in diameter.
2. The isthmus, the part immediately lateral to the uterus, 2-3 cm in length and 2 mm in diameter.
3. The ampulla, the widest part about 5 cm in length.
4. Infundibulum or fimbriated end, it has an opening, the abdominal ostium which is surrounded by a number of finger like processes or fimbriae, one of these is longer than the others and is adherent to the ovary (fimbria ovarica).

At the uterotubal junction there is a sphincter to delay the passage of the fertilized ovum to allow for its maturation and to prevent reflux of blood into the peritoneal cavity during menstruation.

Structure

1. Mucous membrane or endosalpinx. It is thrown into longitudinal folds (plicae). It is lined by columnar cells. Some of the cells are ciliated, others are secretory and others are "peg-shaped". These are immature or senile forms of the other types.
2. Muscle layer. Made of outer longitudinal and inner circular smooth muscle fibres.
3. Peritoneal coat. Which is absent along the attachment of the broad ligament.

Blood Supply

Ovarian and uterine arteries. Gangrene of the tube never occurs because of this double blood supply.

Lymphatic Drainage

The same as the ovary.

Nerve Supply

From the ovarian plexus of nerves.

THE OVARY

Anatomy

Oval solid structure. 1.5 cm in thickness, 2.5 cm in width and 3.5 cm in length. Each weighs 4-8 gm. The ovary has an upper pole attached to the pelvic wall by the infundibulopelvic ligament, lower pole suspended to the cornu of the uterus by the ovarian ligament, medial surface, lateral surface, anterior border, attached to the posterior layer of the broad ligament by a fold of peritoneum called the mesovarium and a posterior free border. The ovary lies in a depression on the lateral pelvic wall called "fossa ovarica" which is bounded in front by the obliterated umbilical artery and behind by the ureter and internal iliac artery. The ovary is the only organ in the abdomen which is not covered by peritoneum.

Structure

It is divided into 3 regions. The hilum which gives attachment to the mesovarium and through which pass blood vessels, lymphatics and nerves. The medulla which consists of connective tissue and is surrounded by the cortex. The cortex contains primary follicles in various stages of development. The ovary is covered by the tunica albuginea which is a dense layer of connective tissue. A single layer of cubical epithelium covers the tunica called germinal epithelium which disappears at puberty. At birth each ovary contains about one million primary follicles.

The function of the ovary is production of ova and secretion of hormones, oestrogens, progesterone and androgens (testosterone, androstenedione and dehydroepiandrosterone). It also produces inhibin, activin, and relaxin hormones.

Blood Supply

Ovarian and uterine arteries.

Lymphatic Drainage

- (1) Lymphatics accompany the ovarian blood vessels to reach the aortic lymph nodes;
- (2) obturator, internal, external and common iliac lymph nodes on the same side of the pelvis;
- (3) inguinal lymph nodes by lymphatics which accompany the round ligament.

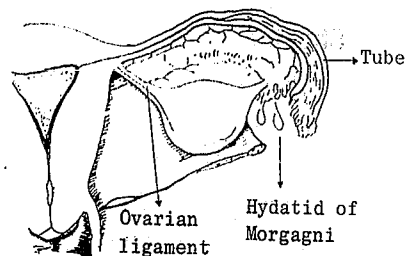


Fig.8. Broad ligament from behind

Nerve Supply

The ovary is supplied by the ovarian plexus of nerves which accompanies the ovarian vessels. The sympathetic nerve fibres arise from ganglia in the celiac and renal areas, and follow the ovarian vessels to reach the ovary and fallopian tube. The sensory fibres reach T-10 and T-11. The parasympathetic fibres are derived from the 2nd, 3rd, and 4th sacral nerves.

The Pelvic Floor

It consists of the following structures from above downwards:

(1) The pelvic peritoneum; (2) extraperitoneal connective tissue; (3) the levator ani muscles which form the pelvic diaphragm; (4) the perineal muscles which include the superficial and deep transverse perineal muscles; the bulbocavernosus, the ischiocavernosus, and the external anal sphincter; (5) subcutaneous fat and fascia; (6) perineal skin.

Notes for the postgraduate

- Superficial transverse perineal muscle. Arises from the ischial tuberosity, and inserts into the perineal body.
- Deep transverse perineal muscle. Arises from the ramus of the ischium, and inserts into the perineal body.
- Bulbocavernosus (bulbospongiosus) muscle. Arises from perineal body and anococcygeal raphe and inserts into the body of the clitoris. It compresses the vestibular bulb, and dorsal vein of the clitoris to maintain its erection (vaginal sphincter).
- Ischiocavernosus muscle. Arises from the ischial tuberosity and ramus of the ischium, and inserts into the undersurface and sides of the crus of the clitoris. It compresses the crus and maintains erection of the clitoris
- The perineal body. It is a pyramidal elastic fibromuscular mass, rich in elastic tissue, and lies between the anal canal and lower third of the vagina. It receives the insertion of the superficial and deep transverse perineal muscles, the bulbocavernosus muscles, the external anal sphincter muscle, and fibres from levator ani muscles.

The Levator Ani Muscle

It is composed of three parts the pubococcygeus, the iliococcygeus and the ischiococcygeus (coccygeus).

The Pubococcygeus

Arises from the back of the body of the pubic bone and meets its fellow of the opposite side in the middle line. It is pierced by the urethra, vagina and rectum. Some of the fibres are inserted into the urethral, vaginal and rectal walls and are known as pubourethralis, pubovaginalis and puborectalis muscles. The remaining fibres are inserted into the side of coccyx and anococcygeal raphe and known as the pubococcygeus proper. The fibres which decussate between the vagina and rectum are called the fibres of Lushka and they form a strong vaginal sphincter. The fibres decussating between the vagina and urethra are called Bolkagoff fibres.

The Iliococcygeus

Arises from the white line (arcus tendineus) which is a thickening in the obturator fascia and is inserted into the side of the coccyx. The obturator fascia covers the obturator internus muscle.

The Ischiococcygeus

Arises from the ischial spine and is inserted into the side of the coccyx and last piece of sacrum.

Nerve Supply

The perineal branch of 4th sacral nerve which reaches the superior surface of the muscle, and inferior haemorrhoidal nerve (from pudendal nerve) which reaches the inferior surface.

Actions

(1) Support of pelvic organs including the bladder, vagina, uterus, and rectum; (2) sphincteric action for the urethra, vagina and rectum; (3) it is responsible for internal rotation of the head during labour.

Notes

- Injury of levator ani during labour may lead to genital prolapse and stress urinary incontinence.
- The anococcygeal raphe is a midline fibrous band extending from anal canal to the coccyx.

THE PELVIC URETER

Anatomy

The pelvic portion of the ureter is 12-15 cm long. It is about the same length as the abdominal part. Diameter about 3 mm. It enters the pelvis by crossing the end of the common iliac artery and runs downwards into the pelvis anterior to the internal iliac artery and behind the ovarian fossa. When it reaches the ischial spine; it runs forwards and medially towards the bladder passing in the base of the broad ligament in the ureteric canal and below the uterine artery (water "urine" flows under the bridge). In the later part of its course, the ureter lies 2 cm lateral to the cervix (supravaginal part) and 2 cm above the vaginal vault.

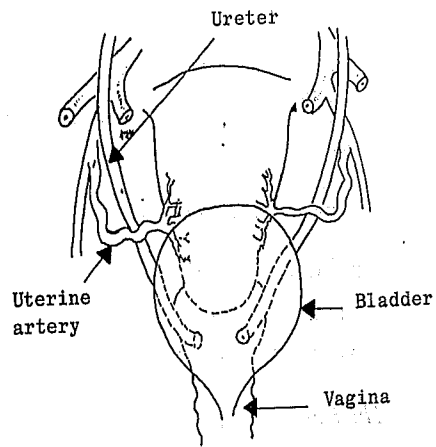


Fig.9. Pelvic ureter

Blood Supply

The pelvic ureter is supplied by a branch from the internal iliac or common iliac artery or lower end of aorta, it also receives branches from the uterine, vaginal, middle rectal and superior vesical arteries.

Dangerous Points of The Ureter

During gynaecological surgery the ureter is liable to be injured at the following sites: (1) at clamping of the infundibulopelvic ligament; (2) at clamping of the uterosacral ligament; (3) when applying the clamp to the uterine artery during hysterectomy; (4) during separation of the bladder from the vagina; (5) during removal of a broad ligament tumour or cervical fibroid which displaces the ureter from its normal site; (6) while closing the peritonum of the pelvic

floor after hysterectomy; (7) in presacral sympathectomy where the ureters are in relation to the common iliac arteries; (8) in vaginal operations for prolapse.

Methods for Protection of Ureter During Pelvic Surgery

(1) Intravenous pyelography is performed before operation when the ureter is liable to be displaced by the pelvic pathology as in case of a broad ligament tumour or cervical fibroid. This will show the site of the ureter; (2) a ureteric catheter is inserted immediately before operation to allow palpation of the ureter; (3) exposure of the ureter at the pelvic brim and its course is followed downwards; (4) pedicles and ligaments should be clamped under vision and not blindly; (5) subcapsular removal of cervical fibroid as the ureter is outside the capsule.

Ectopic Ureter

The ureter may open in the vestibule which is the commonest abnormal site. Other sites include the urethra, vagina, cervix and uterine body.

Causes of Compression of the Ureter

(1) Pregnancy after the 16th week. The ureters are compressed against the pelvic brim; (2) pelvic tumour especially cervical and broad ligament fibroid; (3) cervical carcinoma infiltrating the parametrium; (4) parametric fibrosis following radiation used for the treatment of malignant lesions as cervical carcinoma; (5) second and third degrees of uterine prolapse.

DEVELOPMENT OF THE FEMALE GENITAL ORGANS

1. The two müllerian (paramesonephric) ducts form the tubes, uterus and the upper two-thirds of the vagina. The lower third of the vagina is developed from the urogenital sinus. This sinus appears as a depression in the caudal end of the embryo and deepens to communicate with the upper part of vagina.
2. The vulva develops from the genital tubercle and genital folds. The genital tubercle appears as a mass of tissue at the caudal end of the abdominal wall and will form the clitoris. Also a longitudinal groove appears on the undersurface of the genital tubercle called urethral groove. This has a urethral fold on each side. The urethral folds will form the labia minora in the female and penile urethra in the male. The urethral groove forms the vestibule. Two genital (labioscrotal) folds appear around the genital tubercle and pass upwards to form the mons veneris and backwards on either side of the urogenital sinus to form the labia majora. The membrane covering the urogenital sinus breaks down and its edges form the hymen. The Bartholin glands and Skene tubules develop as outgrowths of the urogenital sinus.
3. The external genital organs are recognised as female at about 12 weeks of pregnancy, and as male at about 14 weeks when the labio-scrotal folds fuse. If a testis is present it produces testosterone and anti-müllerian hormone (factor). Testosterone is reduced by the 5α -reductase enzyme to form dihydrotestosterone (the active hormone) which will lead to formation of male external and internal genitalia. The antimüllerian hormone inhibits the development of the müllerian duct on the same side by a local action on surrounding tissues and not through the blood stream, i.e. a paracrine effect. So absence of the testis leads to formation of female external and internal genital organs.
4. The ovary develops from the genital ridge which is a thickening in the coelomic epithelium on the medial aspect of the intermediate cell mass of mesoderm. It develops at the level of 10th and 11th dorsal segments and descends into the pelvis by traction of the gubernaculum which is a fibromuscular band extending from the lower pole of the ovary to the inguinal region. The gubernaculum will form the ovarian and round ligaments.
5. The Wolffian duct system consists of 2 longitudinal ducts in which open several transverse tubules. In the male these develop into the epididymis, the vasa efferentia, the vas deferens, and seminal vesicles, but in the female, they atrophy and form embryonic remnants between the two layers of the broad ligaments. These are: (a) Kobelt tubules which are found in the outer part of the broad ligament; (b) epoophoron: few tubules lying between the ovary and the tube; (c) paroophoron: tubules lying between the ovary and the uterus; (d) Gartner or Wolffian (mesonephric) duct which runs between the ovary and the tube then lateral to the body of the uterus, then passes through the lateral wall of the cervix then the antero-lateral wall of the vagina and ends at the clitoris. The embryonic remnants may form a paraovarian cyst between the two layers of the broad ligament or Gartner cyst

into the cervix or vagina. Testosterone stimulates the development of the Wolffian ducts. The ducts degenerate in the female due to lack of testosterone.

Note. Hydatids of Morgagni are pedunculated small cysts found near the fimbriae of the tube. They are remnants of the müllerian ducts.

CONGENITAL ABNORMALITIES OF THE OVARIES

(1) Aplasia or complete absence; (2) ovarian (gonadal) dysgenesis in the form of fibrous bands with no follicles "streak gonads" as seen in Turner syndrome; (3) accessory ovaries; (4) failure of descent into the pelvis; (5) ovotestis which is combined ovarian and testicular tissues seen in the true haemaphrodite.

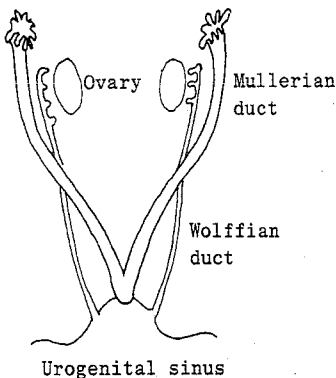


Fig.10. Müllerian and Wolffian systems

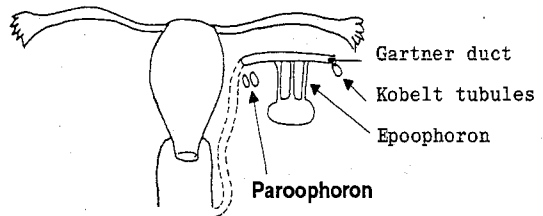


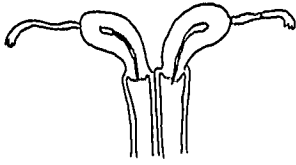
Fig.11. Remnants of the Wolffian system

CONGENITAL ABNORMALITIES OF THE TUBES

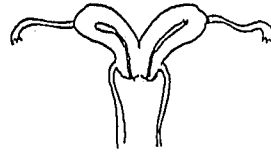
(1) Aplasia; (2) hypoplasia: the tube is long, narrow and tortuous; (3) accessory ostia; (4) congenital diverticulae. These anomalies predispose to tubal pregnancy.

CONGENITAL ABNORMALITIES OF THE UTERUS

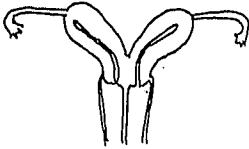
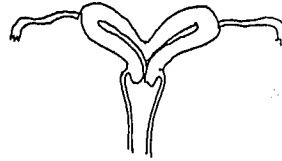
1. **Aplasia, or complete absence.**
2. **Arrest of development:**
 - a. Rudimentary uterus in the form of a solid or hollow muscular nodule.
 - b. Hypoplastic uterus. The total length is less than 6.25 cm (2.5 inches).
 - c. Uterus unicornis. The development of one müllerian duct is completely arrested, so there is only one horn.
 - d. Uterus with a rudimentary horn. One müllerian duct is underdeveloped forming a rudimentary horn which is attached to the uterus by a fibrous band or may communicate with its cavity.
3. **Abnormalities due to incomplete fusion of the müllerian ducts:**
 - a. Uterus didelphys. The 2 müllerian ducts remain separate so that each duct forms a tube, body, cervix, and vagina. The two cervices are at least 2 cm apart.



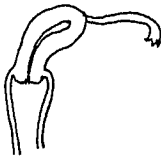
Uterus didelphys



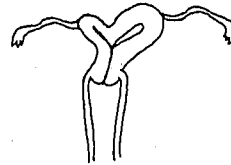
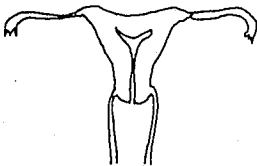
Uterus bicornis bicolis

Uterus bicornis bicolis
with septate vagina

Uterus bicornis unicolis



Uterus unicornis

Uterus with a rudimentary
horn

Arcuate uterus



Subseptate uterus

Fig.12. Congenital uterine abnormalities

- b. Uterus bicornis bicollis. Two uterine bodies and two cervices which are attached together (pseudo-didelphys).
 - c. Uterus bicornis unicollis. Two bodies and one cervix.
 - d. Arcuate uterus (uterus cordiformis); with a depression at the fundus.
 - e. Septate and subseptate uterus.
4. **Congenital elongation of the portio vaginalis of the cervix.** It may be so elongated that the cervix appears from the vagina.

Disorders Associated with Congenital Abnormalities of the Uterus

1. Spasmodic dysmenorrhoea occurs with hypoplastic uterus. One sided dysmenorrhoea occurs with bicornuate uterus when one horn is underdeveloped and with uterus unicornis.
2. Menorrhagia may occur with a bicornuate uterus due to increased surface area of endometrium.
3. Infertility because of uterine hypoplasia or dyspareunia caused by longitudinal vaginal septum.
4. Ectopic pregnancy may occur in the rudimentary horn.
5. Abortion and preterm labour because of uterine hypoplasia, congenital weakness of uterine isthmus (incompetent cervix) and placentation on a uterine septum which may have poor blood supply (placental insufficiency).
6. Malpresentation of the fetus as breech or transverse lie. Habitual malpresentation suggests uterine malformation as bicornuate, septate and subseptate uterus.
7. Uterine inertia during labour due to uterine hypoplasia.
8. Labour may be obstructed by the nonpregnant horn of a bicornuate uterus or by a longitudinal vaginal septum.
9. Placenta accreta when the placenta becomes implanted on uterine septum.

CONGENITAL ABNORMALITIES OF THE VAGINA

1. Aplasia. The vagina may be completely absent or is represented by a shallow depression (the part developing from the urogenital sinus).
2. Hypoplasia. The vagina is short and narrow.
3. Transverse or longitudinal septum.
4. Congenital stricture.
5. Double vagina (uterus didelphys).
6. Congenital ureterovaginal, vesicovaginal or rectovaginal fistula.

Absence of the Vagina

Chromosome analysis is performed to exclude testicular feminization (see amenorrhoea). An ultrasound scan of the renal areas should be undertaken because of the frequent association of renal tract anomalies. Vaginal aplasia is treated by:

1. **Frank Nonoperative Method:** Progressively larger dilators are inserted by the patient or husband to gradually stretch the vagina. Pressure is applied with the dilator for 20 minutes daily. A functional vagina can be created within 6 weeks. This method can be tried before surgery.
2. **McIndoe Operation:** A space is dissected between the urethra and bladder anteriorly and the rectum posteriorly. A plastic mould covered by a split-skin graft (0.5 mm thick) is introduced in the cavity and the labia are sutured over it using silk sutures. The mould is removed after 2 weeks, and the vaginal cavity is irrigated with warm saline solution and inspected. The patient is given a new mould which is used until she starts intercourse, otherwise the vagina will become stenosed (the best dilator is the husband penis). Each night the patient removes the mould, washes it with an antiseptic solution as Betadine before re-insertion.
3. **Williams Operation:** A U-shaped incision is placed over the perineum with the vertical limbs placed over the labia majora. The inner edges are at first sutured together in the midline using chromic catgut; then the outer edges are sutured to make a tube for intercourse.
4. **Thabet Operation:** Like Williams operation, but the transverse limb of the U-shaped incision is placed over the symphysis pubis. Semen will not collect in the created tube.

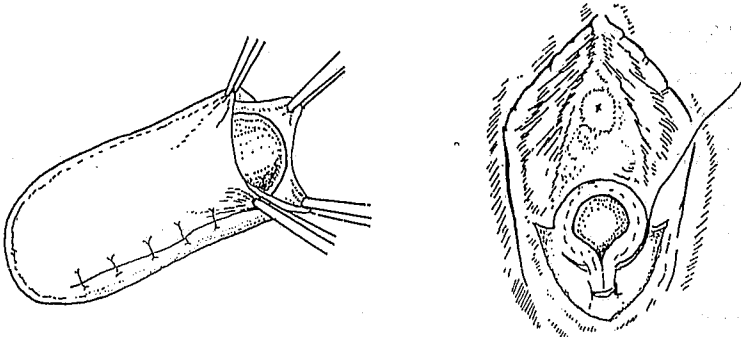


Fig.13. McIndoe operation

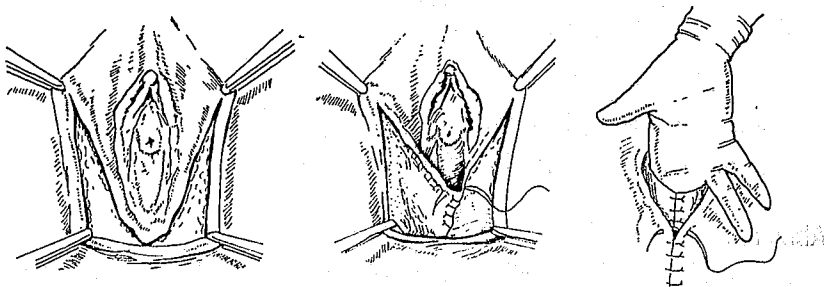


Fig.14. Williams operation

The Mayer-Rokitansky-Kuster-Hauser Syndrome

It is due to failure of development of the müllerian ducts (müllerian agenesis). The vagina is absent or represented by a shallow depression (part developed from urogenital sinus). The uterus is absent or rudimentary. Fallopian tubes are absent or rudimentary. Ovaries are normal because the ovary develops from the genital ridge and not from the müllerian duct. Renal and skeletal abnormalities are frequent (30%, and 15% respectively).

CONGENITAL ABNORMALITIES OF THE VULVA

1. Hypoplasia. Infantile vulva as in Turner syndrome.
2. Cysts as congenital dermoid cyst which occurs only in the midline.
3. Accessory nipple or breast. The breasts and vulva lie in the milk line which extends from the axilla to the vulva.
4. Hypertrophy of the clitoris (clitoromegaly) which is usually associated with other manifestations of virilism.
5. Hypertrophy of one or both labia minora (dog-ear labia minora). This may be congenital or acquired due to frequent masturbation. Also some tribes in Africa attach a weight to the labium minor to make it hanging down as a feature of beauty.
6. Ambiguous external genitalia as in congenital adrenal hyperplasia.
7. Double vulva. There is duplication of the genital tract, urethra, and urinary bladder.

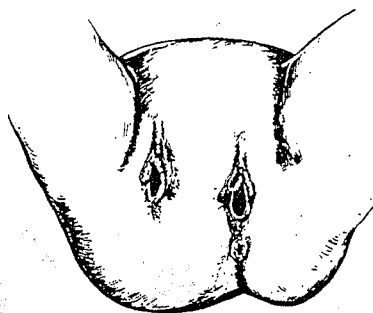


Fig. 14-2. Double vulva.

IMPERFORATE HYMEN

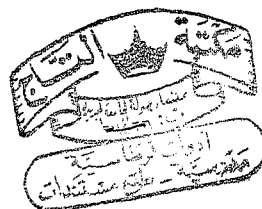
Pathology

The menstrual blood accumulates in the vagina every month leading to its distension and formation of a swelling (haematocolpos). In long-standing cases the blood distends the uterus (haematometra) and later the tubes (haematosalpinx). Some of the blood is absorbed and so the retained fluid is dark brown and thick.

Symptoms

The patient complains of one or more of the following:

1. Primary amenorrhoea.
2. Lower abdominal pain recurring every month.
3. An abdominal swelling.
4. Urinary symptoms as dysuria, acute retention or chronic retention with overflow caused by stretching and compression of the urethra by the distended vagina. The first symptom of imperforate hymen is usually primary amenorrhoea.



Signs

1. In long-standing cases an abdominal mass is felt arising from the pelvis. It is tense cystic and has a limited mobility. The uterus may be felt as a small firm nodule on the top of the mass.
2. Vaginal examination shows a bulging blue closed hymen.
3. Rectal examination shows a tense cystic mass anterior to the rectum and continuous with the abdominal swelling.

Treatment

Under general anaesthesia a cruciate incision is made in the hymen followed by excision of the edges. If it is desired to preserve the hymen, a circular incision is made after applying traction on the centre of the hymen. Antibiotics are given because blood is a good medium for infection and the vaginal resistance is low due to absence of Döderlein bacilli.

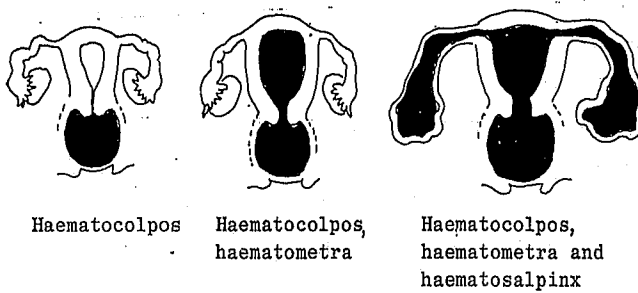


Fig.15. Imperforate Hymen



PHYSIOLOGY OF MENSTRUATION

Menstruation means cyclic uterine bleeding caused by shedding of progestational endometrium. It occurs between menarche (first menstruation) and menopause (physiological cessation of menstruation). Cyclic uterine bleeding caused by shedding of proliferative endometrium is known as pseudomenstruation or anovulatory bleeding.

CHARACTERISTICS OF NORMAL MENSTRUATION

1. Menarche between 10-16 years average 13.
2. Duration of the bleeding 2-7 days (<2 days is hypomenorrhoea and >7 days is menorrhagia).
3. Length of cycle 3-5 weeks, average 4 weeks, estimated from the first day of menstruation to the first day of the next period (<3 weeks is polymenorrhoea and >5 weeks is oligomenorrhoea). Only 15% of women have the typical 28-day cycle.
4. Amount; 30-60 ml, during the whole period. The woman usually uses 3 napkins daily (2 by day and 1 by night). Loss more than 80 ml is abnormal (menorrhagia), and less than 30 ml is hypomenorrhoea.
5. Normally the menstrual blood does not coagulate. At first the blood coagulates in the uterine cavity but is rapidly liquefied by a fibrinolysin enzyme (plasmin) secreted by the endometrium and so the blood becomes devoid of fibrinogen. However, if bleeding is severe or fibrinolysin is deficient, blood clots are passed. In fact, the fibrinolytic system is activated by cell necrosis.
6. The menstrual discharge consists of blood rich in leucocytes, endometrial fragments, cervical mucus, desquamated vaginal epithelial cells, bacteria and enzymes. It also contains prostaglandins, enzymes as alkaline and acid phosphatase.
7. Many women suffer mild symptoms for 7-10 days before menstruation termed "menstrual molimina" which are relieved once menstruation occurs. The symptoms include heaviness in the breasts, irritability or depression. If these symptoms are exaggerated, the condition is called premenstrual syndrome.

THE HYPOTHALAMIC-PITUITARY AXIS

The hypothalamus secretes hormones (factors) which control the activity of the pituitary gland. We have gonadotrophin releasing hormone (GnRH), and prolactin inhibiting hormone which is dopamine. The GnRH stimulates the production of both the follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the basophil cells of the anterior pituitary. Because it secretes more LH than FSH, the GnRH is often called leuteinizing hormone releasing hormone (LHRH). The GnRH is secreted in a pulsatile manner every 60-90 minutes in the follicular phase and every 120-180 minutes in the luteal phase, and reaches the anterior pituitary via the hypophyseal portal vessels.

THE OVARIAN CYCLE

In the first half of the menstrual cycle, the anterior pituitary secretes both FSH and LH. The FSH stimulates the growth of several primary follicles in both ovaries (100-1000). However, only one follicle reaches maturity and forms a graafian follicle which secretes increasing amount of oestrogen (oestradiol). The oestrogen level reaches a peak about 48 hours before ovulation (day 12). This oestrogen peak stimulates increased secretion of LH which reaches a peak about 36 hours before ovulation. The LH peak (surge) leads to ovulation and corpus luteum formation. The LH maintains the growth of the corpus luteum and stimulates it to secrete oestrogen and progesterone. When progesterone reaches a high level it inhibits the secretion of LH. This is followed by degeneration of the corpus luteum. This leads to a drop in the level of oestrogen and progesterone causing separation of the endometrium and menstruation. Also the drop in the level of these hormones stimulates the hypothalamus to secrete more GnRH and thus a new cycle is started in. The life span of the corpus luteum is 14 ± 2 days.

Notes

- Inhibin is a water soluble glycoprotein hormone, secreted by the granulosa cells and inhibits the secretion of FSH and may be involved in the process of follicular atresia. Also secreted by Sertoli cells of the testes.
- Activin is a hormone derived from the ovary and stimulates the secretion of FSH.
- Oestrogen is responsible for the LH surge while progesterone is responsible for FSH surge which also occurs at midcycle.
- Ovulation is due to LH peak. The true mechanism of follicular rupture is unknown.

It may be due to increased intrafollicular pressure, or digestion of collagen fibres in the follicular wall by the proteolytic enzymes. These enzymes are present in the follicular fluid and activated by LH. Also under the influence of LH, prostaglandins increase in the follicular fluid. The prostaglandins may stimulate contraction of smooth muscle fibres in the ovarian stroma leading to follicular rupture.

- When pregnancy occurs, the fertilized ovum secretes human chorionic gonadotrophin (HCG) which stimulates the corpus luteum to grow and form the corpus luteum of pregnancy. This degenerates at 12 weeks when the placenta is formed to carry out its function (secretion of oestrogen and progesterone).
- The mature graafian follicle is 18-24 mm in diameter and consists of (1) ovum; (2) perivitelline space; (3) zona pellucida which is a mucopolysaccharide membrane; (4) corona radiata; (5) cumulus oophorus; (6) cavity filled with liquor folliculi; (7) granulosa cells; (8) theca interna cells; (9) theca externa cells.
- Oestrogen is secreted by the granulosa and theca interna cells of the graafian follicle, the luteinized granulosa cells (lutein cells) and luteinized theca interna cells (paralutein cells) of the corpus luteum, and possibly by stroma cells of the ovary. Progesterone is secreted by the granulosa lutein and theca lutein cells of the corpus luteum.
- The ovary forms oestradiol and oestrone but mainly oestradiol. Oestriol is a metabolite of oestradiol and oestrone and is not formed by the ovary.
- The corpus luteum secretes oestrogen, progesterone, inhibin, and relaxin.

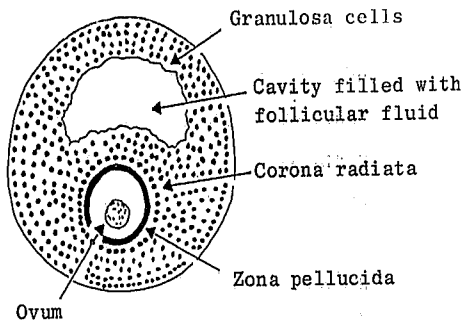


Fig.16. Mature graafian follicle

THE ENDOMETRIAL CYCLE

The changes which occur in the endometrium every month are divided into 3 phases:

1. Menstrual Phase

Two to seven days and during which the superficial functional layer of the endometrium separates leaving the basal layer which contains the basal parts of the glands to allow for regeneration of the endometrium.

2. The Proliferative or Preovulatory Phase

9-10 days, starts after the end of menstruation and ends at the time of ovulation. It is due to the effect of oestrogen produced by the growing graafian follicle and is characterised by:

- a. Thickness of endometrium, 3-4 mm.
- b. Glands are increased in number and length, but remain tubular.
- c. The epithelial cells become low columnar.
- d. Stroma cells increase in size and become globular.
- e. Vascularity is increased.

3. Secretory or Postovulatory Phase

14 $\pm$ 2 days. Its duration is fixed irrespective of the length of the cycle. It begins at ovulation and ends at the onset of menstruation. The endometrium is under the influence of oestrogen and progesterone produced by the corpus luteum and is characterised by:

- a. Thickness of endometrium, 6-8 mm.
- b. Glands continue to grow and become tortuous so that they have a corkscrew or saw-toothed appearance in longitudinal section. The lumen is distended with secretion (glycogen and mucin).
- c. The epithelial cells become high columnar, secretory granules appear at first as subnuclear vacuoles and later as supranuclear vacuoles.
- d. Stroma cells increase in size, become closely packed together and polygonal. The stroma becomes differentiated into three layers:
 - i. Superficial compact layer around the necks of the glands. The stroma cells are closely compacted together.
 - ii. Middle spongy layer around the distended lumens of the glands.
 - iii. Deep compact layer around the basal parts of the glands. The stroma shows oedema, and infiltration with polymorphs and lymphocytes.
- e. Vascularity increases greatly and two types of arterioles can be differentiated:
 - i. Basal arterioles which are short, straight, anastomose freely and supply the basal part of the endometrium.
 - ii. Spiral arterioles which run spirally to supply the superficial layer of the endometrium. They are end arteries and do not anastomose with each other.

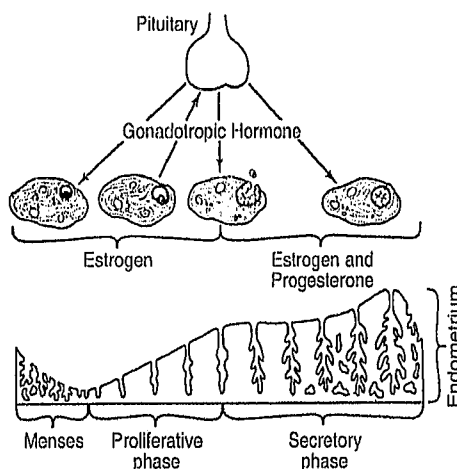


Fig. 17. Ovarian and endometrial cycle.

MECHANISM OF MENSTRUATION

When the corpus luteum degenerates, there is a drop in the level of oestrogen and progesterone leading to reduced oedema and shrinkage of the endometrium causing increasing coiling of the spiral arterioles, ischaemia and necrosis of the superficial and middle layers of the endometrium. The necrotic areas separate leading to bleeding. However, the exact mechanism of menstruation is not yet fully understood. The basal layer of endometrium is not involved because it is supplied by the basal arterioles which anastomose freely. Normally, the endometrium contains prostaglandins (PG) which show a marked increase immediately before and during menstruation. PGF_2 alpha causes vasoconstriction and myometrial contraction and thromboxane A_2 causes vasoconstriction and aggregation of platelets to form thrombi. In this way the menstrual blood loss is reduced. However, in case of endometrial dysfunction, the endometrium secretes more PGF_2 which is vasodilator and prostacyclin which causes vasodilatation and prevents aggregation of platelets thus resulting in menorrhagia.

CYCLIC CHANGES IN CERVICAL MUCUS

In the follicular phase and under the influence of oestrogen, the cervical mucus becomes excessive, watery, less viscid, clear, acellular, stretchable and shows a positive fern test (see infertility). These changes are maximum at the time of ovulation. In the luteal phase, progesterone makes cervical mucus scanty, thick, viscid, cellular, nonstretchable and gives a negative fern test.

CYCLIC CHANGES IN THE VAGINA

Under the influence of oestrogen, the vaginal smear shows many cells with acidophilic cytoplasm and pyknotic nucleic (small and dark). The back ground is clear with few leucocytes. During the luteal phase, there are many intermediate cells with folded edges (navicular cells), basophilic cytoplasm and vesicular nuclei and are clumped together. The background is misty with many leucocytes.

PUBERTY

It is a physiological phase lasting 2 to 5 years, during which the genital organs mature. The manifestations of puberty in the female include menarche, appearance of secondary sex characters, physical development and psychological changes. Secondary sex characters include development of the breast, appearance of pubic and axillary hair.

The first sign of pubertal development is usually breast growth (thelarche), followed by appearance of pubic hair (pubarche), then axillary hair, then menarche. The mean interval between breast budding and menarche is 2.5 years with a standard deviation of about one year.

Note. Adrenarche means increased activity of the suprarenal cortex at puberty with increased production of adrenal androgens which lead to appearance of pubic and axillary hair.

FEMALE PRECOCIOUS PUBERTY

Definition

It means menarche or appearance of any of the secondary sex characters before the age of 8 years. This applies to North America, as the age of precocious puberty depends upon the population and it is more than 3 standard deviations (3 years) below the mean for the population to which the child belongs.

Types

1. **True (central) precocious puberty.** It is due to increased production of pituitary gonadotrophins.
2. **False (peripheral) precocious puberty.** It is of peripheral origin. It is due to secretion of sex hormones; oestrogen or androgen which is not dependent on pituitary gonadotrophins as in case of oestrogenic or androgenic ovarian tumours. False precocious puberty may be isosexual or heterosexual. A girl who feminizes early is defined as having isosexual precocious puberty. A girl who virilizes early is defined as having heterosexual precocious puberty.
3. **Incomplete precocious puberty.** In this case only one pubertal change as breast development is present before the age of 8 years without the presence of any other pubertal changes and in absence of increased oestrogen production. The other pubertal changes occur at the normal age. Incomplete forms of precocious puberty include premature thelarche (unilateral or bilateral), premature pubarche, and premature adrenarche with appearance of pubic and axillary hair.

Aetiology

1. **Constitutional or idiopathic.** In most cases of precocious puberty (90%) no cause is found. For some unknown reason the hypothalamus stimulates the pituitary gland to secrete its gonadotrophic hormones. There is normal menstruation and ovulation. Pregnancy can occur at young age.

2. **Organic lesions of the brain.** The next common cause. Organic lesions affecting the midbrain, hypothalamus, pineal body, or pituitary gland may lead to premature release of pituitary gonadotrophins. Examples include traumatic brain injury, meningitis, encephalitis, brain abscess, brain tumour as glioma, craniopharyngioma, and hamartomas.
3. **McCune-Albright syndrome.**
4. **Adrenal causes.** (a) Hyperplasia, adenoma, or carcinoma of suprarenal cortex. Congenital adrenal hyperplasia and Cushing syndrome lead to precocious puberty in the male direction, i.e. heterosexual precocious puberty; (b) oestrogen secreting adrenal tumour which is very rare.
5. **Ovarian causes.** (a) Oestrogen producing tumours as granulosa and theca cell tumour; (b) androgen producing tumours as androblastoma; (c) choriocarcinoma because it secretes human chorionic gonadotrophin (HCG) which may stimulate the ovaries to secrete oestrogen; (d) dysgerminoma if it secretes HCG.
6. **Juvenile hypothyroidism.** Lack of thyroxine leads to increased production of thyrotrophin releasing hormone (TRH). The gonadotrophin releasing hormone may also increase leading to increased secretion of pituitary gonadotrophins. In addition to short stature, precocious puberty may occur, also hyperprolactinaemia, and galactorrhoea may occur, as TRH directly stimulates the lactotrophs in the pituitary gland.
7. **Drugs.** Iatrogenic or factitious precocious puberty may follow oral or local administration of oestrogen. A long course of oestrogen cream used for treatment of vulvovaginitis of children may lead to breast development or withdrawal bleeding.
8. **Silver syndrome.** It is a congenital syndrome characterized by a short stature, retarded bone age, and slight or moderate increased gonadotrophin levels which may be associated with precocious puberty.

Diagnosis

1. **History.** It excludes iatrogenic source of oestrogen or androgen. It differentiates between isosexual and heterosexual precocious puberty.
2. **Physical examination.** It diagnoses McCune-Albright syndrome. Neurologic and ophthalmologic examinations exclude organic lesions of the brain.
3. **Special investigations.** These are done according to the history and clinical findings and include:
 - a. Hormonal assay including serum FSH, LH, prolactin, oestradiol, testosterone, 17α -hydroxyprogesterone, TSH, and human chorionic gonadotrophin to diagnose choriocarcinoma.
 - b. Ultrasonography to diagnose ovarian or adrenal tumour.
 - c. Computed tomography or magnetic resonance imaging to diagnose an organic lesion of the brain, or adrenal tumour.

- d. X-ray examination of the hand and wrist to determine bone age. Oestrogen stimulates growth of bone but causes early fusion of the epiphysis. So the child is taller than her peers during childhood, but she is short during adult life. Juvenile hypothyroidism retards bone age, and with Silver syndrome are the only two conditions of precocious puberty in which bone age is retarded and not advanced.

Idiopathic precocious puberty is diagnosed after excluding all other causes.

Treatment

1. Treatment of the cause, e.g., thyroxine for hypothyroidism, removal of ovarian and adrenal tumours.
2. Incomplete forms of precocious puberty do not require treatment, as oestrogen production is not increased.
3. McCune-Albright syndrome is treated with testolactone oral tablets. The drug inhibits the formation of oestrogen from its precursors, so reduces oestrogen level. The dose is 20 mg/kg body weight in 4 divided doses and increased to 40 mg/kg body weight after 3 weeks.
4. Idiopathic type is treated by explanation and reassurance and by giving one of the following drugs which inhibit the secretion of gonadotrophins: (a) gonadotrophin releasing hormone analogues (agonists) which are given as daily nasal spray, intramuscular, or subcutaneous injections every 4 weeks. This is the treatment of choice; (b) medroxyprogesterone acetate tablets (Provera tablets) or intramuscular injection (Depo-Provera); (c) danazol; (d) cyproterone acetate tablets (Androcur). Treatment is given till the age of 12 years (mean age of pubertal development).

McCune-Albright Syndrome

The disease is found more frequently in girls. It consists of a triad of precocious puberty, cystic changes in bones, and café-au lait patches of the skin. The cause of precocious puberty is autonomous production of oestrogen by the ovaries. FSH and LH levels are low. The treatment is testolactone oral tablets which inhibit oestrogen formation by the ovaries.

THE MENOPAUSE AND CLIMACTERIC

The menopause is the permanent cessation of menstruation due to failure of ovarian function. Natural menopause is diagnosed when menstruation has ceased for at least 6 months or 1 year by some gynaecologists in a woman above the age of 40, and in absence of any pathologic cause, so it is a retrograde diagnosis. Menopause is a manifestation of the climacteric which is a transitional phase lasting about 5 years before the menopause and about 5 years after the menopause and during which the ovarian function fails and the genital organs involute.

TYPES OF MENOPAUSE

1. Normal or natural menopause. Occurring between the age of 40 and 55 years with an average of 50 years.
2. Premature menopause. Menstruation ceases before the age of 40. It occurs in about 1% of women below the age of 40.
3. Delayed menopause. Menstruation continues after the age of 55. The causes are: (a) constitutional (a familial or racial tendency); (b) uterine fibroids; (c) diabetes mellitus and; (d) oestrogenic ovarian tumours.
4. Artificial menopause. Caused by surgical removal of both ovaries or their destruction by radium or deep X-ray therapy.

THE MODE OF ONSET OF MENOPAUSE

Menopause may be preceded by (a) hypomenorrhoea; (b) oligomenorrhoea; (c) oligo-hypomenorrhoea; (d) a period of dysfunctional uterine bleeding or (e) menstruation stops suddenly and never recurs. This occurs in about 10% of women.

THE CHANGES ASSOCIATED WITH MENOPAUSE

These are general, local, and hormonal changes.

1. General Changes

- a. Atrophy of the glandular tissue of the breast. However, the breasts may become large and pendulous due to deposition of fat.
- b. Gastrointestinal changes. Appetite may be decreased or increased leading to obesity. There may be various forms of dyspepsia as flatulence and constipation.
- c. Tendency to develop menopausal hypertension. Oestrogen protects against atherosclerosis.
- d. The levels of serum cholesterol and triglycerides rise and the risk of coronary heart disease gradually increases.
- e. Liability to osteoporosis (reduction in the bone mass without a change in the chemical composition of bone). Oestrogen stimulates gut absorption of calcium, reduces calcium loss by kidneys, inhibits the osteoclasts, opposes the action of parathyroid hormone on bone, stimulates calcitonin secretion (calcitonin hormone inhibits the action of

osteoclasts), and facilitates conversion of vitamin D into the active form (1,25-dihydroxy vitamin D).

- f. Mild hirsutism usually occurs. Oestrogen production is decreased leading to decreased synthesis of sex-hormone binding globulin, and so free testosterone is increased.
- g. Psychological changes as headaches, irritability and depression.

2. Local Changes

- a. The pubic hair becomes scanty, grey or white in colour.
- b. Atrophy of the vulva with loss of subcutaneous fat.
- c. The vagina becomes narrow. The mucosa loses its rugae, becomes smooth, thin with little or no glycogen. The vaginal acidity is reduced, the pH becomes neutral or alkaline. This predisposes to infection and senile vaginitis.
- d. The uterus becomes small and atrophic. The portio vaginalis of the cervix may disappear. Senile endometritis may occur.
- e. The ovaries become small, fibrotic and containing no follicles.
- f. The cervical ligaments become atrophic and this may lead to genital prolapse.
- g. Atrophy of the bladder and urethral mucosa. This may lead to frequency of micturition, urgency, stress incontinence and recurrent attacks of cystitis and urethritis.

3. Hormonal Changes

- a. Oestrogen level is low due to absence of ovarian follicles. After menopause the ovary and adrenal glands secrete androgens (mainly androstenedione) which is converted into oestrone. This conversion takes place mainly in body fat but also in the liver, skin and muscles. Because of this peripheral (extraglandular) conversion only 10-50% of women after menopause have oestrogen deficiency. Oestrone is the main oestrogen in postmenopausal women and part of it is converted into oestradiol.
- b. There is increase in the serum levels of follicle stimulating hormone (FSH) and luteinizing hormone (LH). A serum level of FSH above 40 mIU/ml indicates cessation of ovarian function and it precedes the rise in LH level.

Notes for the postgraduate

1. Oestradiol comes mainly (90%) from the ovary and a small amount arises by peripheral conversion of testosterone and oestrone.
2. Oestrone arises mainly by peripheral conversion of androstenedione and a small amount comes from the ovary.
3. Testosterone, and androstenedione come from both the ovaries and adrenal glands.
4. Peripheral conversion leads to:
 - Androstenedione → oestrone.
 - Testosterone → oestradiol.
 - Androstenedione ↔ testosterone.
 - Oestrone ↔ oestradiol.
5. After menopause, there is a decrease in the production of inhibin and oestradiol by the granulosa cells in the ovary. Decreased inhibin increases FSH. Decreased oestradiol increases FSH and LH to a lesser extent.

6. After menopause androgen production decreases by 50% due to decrease in both ovarian and adrenal production.

MENOPAUSAL SYNDROME

The menopause is associated with mild or no symptoms in about 70% of cases. The symptoms are moderate in 20% and severe in 10%. The symptoms of menopausal syndrome are:

1. **Cardiovascular (vasomotor);** as palpitation, hot flushes, and night sweats. The hot flushes or flashes are present in about 75% of postmenopausal women. They usually disappear after 1-2 years even without treatment as the body adjusts itself to the new low oestrogen level. However, about 25% of cases will continue to have the flushes for more than 5 years. The hot flush is a sensation of heat felt in the chest, neck, face, and head and may spread all over the body. It is due to attacks of subcutaneous vasodilatation and is usually accompanied with tachycardia and excessive sweating. Vasodilatation is followed by vasoconstriction, so after a flush comes a cold shiver. The hot flush lasts for seconds, minutes, and rarely for one hour but usually 3 minutes. Flushes vary in number from one or two in 24 hours to one every 15-30 minutes in a day. The true cause of hot flushes is unknown but most probably due to sudden drop in oestrogen level. However, other sex hormones as androgens and progesterone may be responsible. Progestogens suppress hot flushes but are less effective than oestrogens. Night sweats are the counterpart of hot flushes felt during the daytime (waking time).
2. **Gastrointestinal.** Appetite may be decreased or increased leading to obesity. There may be various forms of dyspepsia as flatulence and constipation.
3. **Psychological;** as headaches, depression, irritability, lack of concentration, poor memory and insomnia. Insomnia is usually the result of night sweats.
4. **Metabolic;** as obesity, osteoporosis, joint pains and backache due to laxity of ligaments and decreased muscular strength.
5. **Sexual.** The libido is unchanged in most cases, but may be increased or decreased. Decreased libido reflects an aging process.
6. **Genitourinary.** The woman may suffer from senile endometritis, senile vaginitis, dryness of the vagina and dyspareunia. Urinary symptoms in the form of frequency, urgency, stress incontinence, and recurrent attacks of cystitis and urethritis.

Note. Oestrogen has nothing to do with libido. It is testosterone which increases the libido.

Treatment

1. General

Explanation and reassurance because menopause is a change in life and not an end of life. Avoid factors which can precipitate hot flushes as hot weather, hot baths, nervousness, excessive intake of coffee or tea, excessive blankets and coverings during sleep.

2. Diet

Control of diet with less fat to avoid obesity. Increase calcium intake and exercise to guard against osteoporosis. If the woman is not receiving oestrogen therapy supply her with extra 1000 mg calcium daily so that the total intake becomes 1500 mg as the normal diet contains 500 mg of calcium. If she is on oestrogen therapy supply her with extra 500 mg calcium.

3. Medical

Symptomatic treatments as sedatives, tranquilizers, stimulants for depression and beta-blockers for tachycardia and palpitation.

4. Hormonal

- a. Oestrogens. Oestrogen is given alone if the uterus has been removed as there is no risk of endometrial hyperplasia and endometrial carcinoma. The indications for oestrogen therapy are:
 1. The presence of menopausal symptoms in the form of (a) hot flushes; (b) senile vaginitis; (c) atrophic vagina causing dyspareunia; (d) urinary symptoms as frequency, stress incontinence, recurrent cystitis and urethritis; (e) psychological disturbances. Treatment is given for at least one year to prevent recurrence of symptoms.
 2. Premature menopause as this predisposes to osteoporosis. Treatment is given at least till the age of 50 years (average age of menopause). This reduces the risk of osteoporosis by 50-60%.
 3. Treatment of osteoporosis.
- b. Combined oestrogen-progestogen therapy. Given if the woman has the uterus as progestogens protect against endometrial hyperplasia, and endometrial carcinoma.
- c. Progestogens alone are given to control hot flushes when oestrogen is contraindicated as in case of acute or chronic liver disease. Progestogens suppress hot flushes but are less effective than oestrogens (medroxyprogesterone acetate tablets, 10-30 mg daily).
- d. Tibolone (Livial). It is a synthetic drug taken orally, one tablet daily. It has oestrogenic, progestogenic, and weak androgenic effects (hormones normally produced by the ovary). The androgenic effects improve libido. About 15% of patients experience irregular uterine bleeding.

5. Nonhormonal Drugs to Control Hot Flushes

Some drugs are tried to control hot flushes if oestrogens are contraindicated. These include the antihypertensive drugs methyl dopa and beta-blockers. Also Agreal capsules (anxiolytic sedative) can be used. They are less effective than oestrogens and have their side effects.

Treatment of Postmenopausal Osteoporosis

In addition to oestrogen, calcium, vitamin D, fluoride, calcitonin and bisphosphonates are used for the treatment of postmenopausal osteoporosis. Calcium slows bone loss but does not increase bone mass. Fluoride is the only known agent which increases bone mass. Bisphosphonates inhibit the osteoclasts and reduce bone resorption. Alendronate (Fosamax) is the most potent bisphosphonate and is given orally. The dose is 5 mg daily for prevention, and 10 mg daily for treatment.

Notes

- Osteopenia means borderline reduction in bone mass. Osteomalacia means increased softness of bone due to reduced mineral content leading to deformities. It is the adult form of rickets.
- The bone formed by sodium fluoride is fragile and more liable to fracture.

PREMATURE MENOPAUSE (PREMATURE OVARIAN FAILURE)

Definition

It means cessation of menstruation (ovarian function) before the age of 40 years due to depletion of ovarian follicles or failure of the primordial follicles to respond to gonadotrophins. It is a condition of hypergonadotrophic-hypogonadism.

Incidence

Premature ovarian failure (POF) affects about 1% of all women under the age of 40.

Aetiology

1. Idiopathic. In most cases no cause is found to explain the increased rate of follicle disappearance.
2. Chromosomal disorders. Some of the mosaic cases of Turner syndrome, pure gonadal dysgenesis, trisomy-18, and trisomy-13.
3. Metabolic disorders. Myotonia dystrophy, 17- α hydroxylase deficiency, and galactosaemia. The galactose metabolites may affect the migration of germ cells to the genital ridge during intrauterine life leading to reduced number of oogonia (ova) in the ovary.
4. Immunological disorders. Di George syndrome and mucocutaneous fungal infections.
5. Autoimmune diseases. As hypothyroidism due to autoimmune thyroiditis, Addison disease, idiopathic thrombocytopenic purpura, and rheumatoid arthritis. These are associated with antiovarian antibodies. Ovarian biopsy shows primordial follicles surrounded by lymphocytes and plasma cells. The exact mechanism of resistance to gonadotrophins is unknown. Autoimmune ovarian failure is known as Blizzard syndrome.
6. Resistant ovary syndrome.
7. Infections. Mumps and pelvic tuberculosis leading to destruction of follicles.
8. Chemotherapy and radiotherapy used for treatment of cancer.

9. Hysterectomy and removal of ovarian cysts may lead to impairment of ovarian blood supply and POF.
10. Smoking leads to premature menopause by 2 years.
11. Undernourishment.
12. Living at high altitudes.

Diagnosis

It is made by the occurrence of amenorrhoea in a woman below the age of 40. The presence of symptoms and signs of oestrogen deficiency as hot flushes. Serum oestradiol is less than 20 picograms/ml and serum FSH is above 40 mIU/ml. If the woman is below the age of 30, chromosomal study should be done to exclude chromosomal anomaly as Turner syndrome. Ovarian biopsy (full-thickness) diagnoses resistant ovary syndrome. The biopsy shows normal number of primordial follicles. In autoimmune disorders the primordial follicles are surrounded by lymphocytes and plasma cells.

Note. Serum FSH between 20 and 40 mIU/ml indicates impending ovarian failure.

Treatment

Oestrogen-progestogen replacement therapy is given to women with POF till the age of 50 years which is the average age of natural menopause to reduce the risk of osteoporosis.

HORMONE REPLACEMENT THERAPY (HRT)

Indications of Oestrogen Replacement Therapy

See before.

Contraindications to Oestrogen Therapy

1. Acute and chronic liver disease.
2. Gallbladder disease. Oestrogen predisposes to cholestatic jaundice and formation of cholesterol stone.
3. Coronary heart disease.
4. Active thrombophlebitis.
5. Recurrent thrombophlebitis and recurrent venous thrombosis.
6. Ophthalmic vascular disease.
7. Existing breast and oestrogen dependent carcinoma.
8. Undiagnosed uterine bleeding.
9. Porphyria.

Diabetes mellitus, and hypertension are not contraindications. Also there is no evidence that oestrogen replacement therapy increases the risk of recurrence after treatment of breast carcinoma.

Advantages of Oestrogen Therapy

1. Relieves menopausal symptoms and improves quality of life.
2. Reduces the risk of osteoporosis by 50-60%.
3. Reduces the incidence of colonic and rectal cancers, but it is not used for prophylaxis.

Complications of Oestrogen Therapy

1. Headache.
2. Breast tenderness and enlargement.
3. Gastric discomfort and nausea.
4. Uterine bleeding.
5. Generalized oedema.
6. Excessive cervical mucus.
7. Increased risk of deep venous thrombosis (2-4 times) and pulmonary embolism (2 times).
This occurs with oral therapy. The risk is present in the first year of use. The risk can be reduced by screening for hereditary deficiency of clotting factors and if present, long-term aspirin is indicated.
8. Gallbladder disease with formation of cholesterol stones and cholestatic jaundice.
9. Slight impairment of glucose tolerance (with oral therapy).
10. Blood pressure may increase (with oral therapy).
11. Endometrial carcinoma. So in the presence of the uterus a progestogen must be given orally for 10-14 days every month (minimal duration for 10 days and optimal duration for 14 days).
12. Slight increase of breast carcinoma if oestrogen is given for more than 10 years. The relative risk is about 1.2. The risk continues for 10 years after cessation of therapy. Progestogens do not oppose the action of oestrogen on breast tissue. In fact oestrogen-progestogen regimen increases the risk of breast cancer beyond that associated with oestrogen alone.

Note. The incidence of endometrial carcinoma will be 4% if the progestogen is given for 7 days, and 2% if given for 10 days, and 0% if given for 14 days.

Regimens of HRT

1. Oestrogen only.
2. Combined oestrogen and progestogen.
3. Progestogen only.
4. Tibolone.

Oestrogen Only

Indicated if the uterus has been removed. In this case a progestogen is not added because there is no risk of endometrial hyperplasia and carcinoma. Also the progestogen may reverse the beneficial effects of oral oestrogens on lipoproteins.

Combined Oestrogen and Progestogen

A progestogen must be added if the uterus is present to prevent endometrial hyperplasia and carcinoma.

Progestogen Only

This is given to control hot flushes when oestrogen is contraindicated as in case of acute and chronic liver disease. Progestogens suppress hot flushes but are less effective than oestrogens.

Medroxyprogesterone acetate (MPA) tablets (Provera tablets) are given as 10-30 mg daily or MPA injection (Depo-Provera) is given 150 mg IM every 3 months.

Tibolone

See treatment of menopausal syndrome.

Oestrogen Only

It is given in the form of oral tablets, skin (transdermal) patch, subcutaneous implant, skin gel, vaginal cream, vaginal tablets, and vaginal ring.

Oral Oestrogens

Conjugated oestrogens (Premarin); the dose is 0.625 mg daily. It is effective in most cases and can be increased to 1.25 mg daily. Another oestrogen is piperazine oestrone sulfate 1 mg daily or oestrinol (Ovestin) 1 mg daily.

Oral therapy is the treatment of choice as it is easy to take, cheaper, and allows good control of the dose.

Transdermal Patch

The patch (Estraderm) is applied twice weekly usually to the buttocks, as the action lasts for 3 to 4 days. It releases oestradiol at a rate of 25, 50, or 100 micrograms per 24 hours. The usual dose is 50 µg/day. It may cause skin reaction in up to 30% of cases. It is more expensive than oral therapy. If the uterus is present, a progestogen is given for 10 days every month, e.g. MPA 10 mg daily for 10 days. Now patches containing oestradiol and a progestogen are available, e.g., Estracombi.

Subcutaneous Implant

Capsules containing 25, 50 and 100 milligrams of oestradiol are available. The 50 mg dose is most commonly used. The capsule is inserted subcutaneously in the abdominal wall using local anaesthesia once every 6 months (4-8 months). In the presence of the uterus a progestogen is given for 10 days each month, or we insert Mirena intrauterine device.

Skin Gel

Gel containing oestradiol is applied to the skin of the arms or legs. The dose is 1-5 mg daily.

Vaginal Cream, Tablet and Ring

For vaginal atrophy and dyspareunia both oral and local oestrogen are given, as oral therapy alone is usually not enough to stimulate growth of vaginal epithelium. Local therapy in the form of vaginal cream (Premarin cream) or vaginal tablet is given for a short course 2-3 months. A vaginal ring (Estring) can be used which releases oestradiol over 3 months.

Oestradiol Nasal Spray

It is used to control hot flushes to avoid the large dose of oestrogen given orally. The dose is 100, 200, 300, or 400 micrograms daily.

Indications of Non-Oral Oestrogen

1. Gastrointestinal problems. Gastric discomfort and the presence of gastritis, ulcer, and malabsorption syndrome.
2. Failure of oral therapy to control symptoms. The parenteral route gives a higher serum oestradiol level.
3. Metabolic disorders. Diabetes mellitus, hypertension, elevated triglycerides and lactose intolerance. Parenteral oestrogen bypasses the liver, so it does not impair glucose tolerance and does not cause hypertension as the liver production of renin substrate and angiotensinogen is not increased. It also lowers the triglycerides. All oral oestrogen and oral progestogen preparations contain lactose as a bulking agent. Hypolactasia (deficiency of lactase activity in the intestine) leads to lactose intolerance and contraindicates oral HRT.
4. History of deep venous thrombosis. Oral oestrogen stimulates the liver to produce clotting factors and inhibits antithrombin III production.
5. Severe osteoporosis. Oestradiol implant gives a high serum oestradiol level with better response.

Combined Oestrogen and Progestogen Therapy

Indicated if the uterus is present.

1. Oestrogen plus cyclic progestogen. A progestogen is given cyclically for 10-14 days every month. An example is to give conjugated oestrogens, 0.625 mg daily and MPA 10 mg daily for 10-14 days. This cyclic progestogen leads to cyclic uterine bleeding (menstruation) in most women. It can also lead to irregular uterine bleeding. Cyclic treatment may be given to perimenopausal women to cause cyclic uterine bleeding.
2. Oestrogen plus continuous progestogen. Conjugated oestrogens, 0.625 mg daily plus MPA 2.5 mg daily. This allows giving a smaller total dose of progestogen to reduce its side effects. This regimen can also lead to irregular uterine bleeding. Continuous treatment is given to women who have been amenorrhoeic for one year.
3. Oestradiol skin patch (Estraderm) plus a progestogen for 10 days every month.
4. Oestradiol-progestogen skin patch, e.g., Estracombi.

5. Progesterone suppositories inserted vaginally or rectally (Cyclogest), or Levonorgestrel intrauterine device (Mirena) can be combined with oestrogen therapy.

Nonhormonal Drugs

Some drugs are tried to control hot flushes if oestrogens are contraindicated. See treatment of menopausal syndrome.

Work up Needed before HRT

1. Detailed history including family history for endometrial and breast cancer.
2. Complete physical examination including the breasts. Blood pressure and weight are recorded.
3. Urine is examined for sugar and protein.
4. Special investigations:
 - a. Fasting blood sugar.
 - b. Serum FSH and oestradiol.
 - c. Lipid profile.
 - d. Endometrial sampling. Done by some gynaecologists in USA.
 - e. Cervical smear.
 - f. Mammogram.
5. Counselling and consent for HRT.

Monitoring of the Patient under Therapy

The patient should be reviewed after:

- Two months: to check side effects, control of symptoms, blood pressure and weight.
- Six months: to ensure that the uterine bleeding is acceptable and to deal with any problem.
- Then every 6 months thereafter: to examine for blood pressure, weight, breasts, and legs.
- Every year, the woman should have a lipogram, mammogram and a cervical smear.

Notes for the postgraduate

1. Conjugated oestrogens are extracted from the urine of pregnant mares. They are a combination of oestrone (50%), equilin, dihydroequilin and other oestrogens.
2. The premenopausal woman needs 1000 mg calcium daily. The postmenopausal woman needs 1500 mg calcium daily. The diet provides 500 mg calcium/d. So after menopause the woman should receive an extra 1000 mg calcium/d if she is not receiving oestrogen therapy and 500 mg/d if she is receiving the therapy.
3. Migraine may or may not be aggravated by HRT, so a trial of treatment is not contraindicated.
4. In menstruating women bone loss occurs at a rate of less than 1% per year. After menopause the rate is 3 to 5% per year.
5. HRT is used by only 38% of women in the United States.

SERMs

SERMs means selective oestrogen receptor modulators. These modulators are nonhormonal compounds different in structure from oestrogens. They stimulate certain – but

not all – oestrogen receptors, hence the name. There are 2 types of oestrogen receptors. Alpha oestrogen receptors present in the breasts and uterus, and beta receptors present in the brain, bone, vagina, urinary bladder, granulosa cells of the ovary, and cardiovascular system. Oestrogen receptors are present in the cell nuclei of target tissues. SERMs include the following:

1. **Tamoxifen (Nolvadex):** It belongs to the first generation of SERMs. It inhibits E receptors in the breasts, but stimulates E receptors in the uterus, bone, and cardiovascular system. It is used in the treatment of breast cancer. However, its use more than 5 years may lead to endometrial hyperplasia, polypsis, carcinoma, sarcomas, adenomyosis, growth of fibroids, and simple ovarian cysts (10%). The latter may be due to direct action causing excessive growth of ovarian follicles.
2. **Clomiphene citrate (Clomid).** It belongs to the first generation of SERMs.
3. **Raloxifene (Evista).** It is the second generation of SERMs. It stimulates oestrogen receptors in bone and vagina, but inhibits oestrogen receptors in the breasts and endometrium. The drug is only used to prevent osteoporosis in postmenopausal women who do not wish to take hormone replacement therapy (HRT) or when it is contraindicated. It does not treat hot flushes, and may increase them. It causes leg cramps in 55% of cases, and slightly increases venous thrombosis. The dose is 60 mg per os daily.
4. **Phyto-oestrogens (Klimadynon).** These are compounds found in certain plants as lentil, peas and soya beans. They have both oestrogenic and antioestrogenic action depending on the target tissue. The oestrogenic effect is weak – about 2% that of oestradiol. These compounds stimulate oestrogen receptors in the brain, and so reduce the number of hot flushes by 50%, also reduce irritability, insomnia, and depression. They also reduce the risk of bone fracture by decreasing osteoclastic activity. They stimulate proliferation of vaginal epithelium, and prevent vaginal dryness, and dyspareunia. They have no effect on breasts or endometrium.

Indications for phyto-oestrogens

1. Women who do not wish to take HRT or when HRT is contraindicated.
2. Women who want to take a natural product for hot flushes.
3. As a supplement to HRT when we do not want to increase the dose of oestrogen.

SECTION II

GYNAECOLOGICAL DIAGNOSIS

HISTORY AND PHYSICAL EXAMINATION

Diagnosis in medicine depends upon the triad of history, physical examination and investigations.

A. HISTORY

1. Personal History

Name, age, marital status, duration of marriage, occupation, nationality, consanguinity, address and telephone number.

2. Complaint

It is taken in the patient own words.

3. Present History

Each complaint is taken in detail. The patient is also asked about urinary symptoms as burning, pain and frequency; and gastrointestinal symptoms as nausea, vomiting, diarrhoea or constipation.

4. Past History

- Past medical history. Ask about the presence of any chronic disease as hypertension, heart disease, diabetes mellitus, renal disease, etc.
- Past surgical history. Ask about any operation done for the patient as appendectomy.
- Hormonal treatment and contraceptive history.
- History of blood transfusion.
- The presence of allergy to drugs, food, etc.
- Exposure to irradiation or radiotherapy.



5. Family History

Ask about conditions that can be inherited as hypertension, heart disease, diabetes mellitus, endocrine disorders, malignant diseases as breast, ovarian, and endometrial carcinoma.

6. Menstrual History

Menarche, duration of menstrual bleeding, length of cycle (D/C), amount (slight, moderate or excessive), the presence of pain and its relation to bleeding, intermenstrual bleeding or discharge. The first day of last menstrual period (LMP).

7. Obstetric History

(a) In each delivery we ask about: (i) duration of pregnancy (preterm, full term, or post-term); (ii) mode of delivery (spontaneous vaginal delivery, by forceps, etc.); (iii) the newborn (male or female, alive or dead); (iv) fetal or maternal complication in the puerperium; (v) time of last delivery. (b) In each abortion, we ask about: (i) duration of pregnancy; (ii) mode of termination (spontaneous or induced); (iii) complication in the postabortive period; (iv) time of last abortion.

8. Sexual History

In case of infertility.

9. Social History

Ask about special habits of medical importance as smoking, alcohol and drugs.

B. PHYSICAL EXAMINATION

I. General Examination

General condition: (good, moderate or bad) and constitution.

Pulse, temperature, blood pressure

Eye examination: Pallor, jaundice, oedema of eye lids

Nose: e.g. saddle nose due to syphilis

Mouth: Tongue, teeth, tonsils

Neck: Thyroid, lymph nodes, congested neck veins

Chest: Heart, lungs, breasts and exclude galactorrhoea

Lower Limbs: Varicose veins, bony deformities, other abnormalities

Note. Six areas of the breast are palpated (four quadrants, area behind the nipple, and axillary tail).

2. Abdominal Examination

The patient should empty her bladder before examination.

- a. **Inspection.** Contour, scar, pubic hair (feminine with an upper straight border, or masculine with a convex upper border), pigmentation as linea nigra, dilated veins, the presence of hernia. To differentiate between an intra-abdominal mass and a mass arising from the anterior abdominal wall, the patient is asked to sit unsupported. If the mass diminishes in size, it is intra-abdominal.
- b. **Palpation.** Superficial to detect tenderness or rigidity, to feel a superficial swelling, arising from the anterior abdominal wall and to gain confidence of the patient and deep palpation to examine the nine areas of the abdomen.
- c. **Percussion.** For any mass present and shifting dullness to detect ascites or internal haemorrhage. A small amount of fluid causes an area of dullness around the umbilicus with the patient in the knee-chest position.
- d. **Auscultation.** If we suspect pregnancy.

3. Pelvic Examination

Vaginal examination includes:

- a. **Inspection.** The various structures of the vulva and perineum are inspected for any abnormality. The patient is asked to cough or strain down to detect prolapse or stress incontinence.
- b. **Digital palpation.** The lubricated index and middle fingers or index finger alone of the gloved right hand are introduced into the vagina until the cervix is reached. The cervix is palpated to detect any abnormality. The anterior, then the posterior vaginal wall is palpated. The urethra is milked from above downwards to detect any discharge. The Bartholin glands are palpated. Normally, the gland is not felt unless diseased and its opening is not seen unless inflamed.
- c. **Bimanual examination.** The two fingers are placed in front of the cervix in the anterior vaginal fornix. The left hand is placed flat on the lower abdomen just above the symphysis pubis. The two hands are pressed together to feel the uterus in between and note any abnormality. If the uterus is retroflexed it cannot be felt through the anterior fornix, but is felt through the posterior fornix. After palpating the uterus, the two fingers are placed in one lateral fornix and the abdominal hand is placed lateral to the uterus to feel the adnexa. Repeat this on the other side. Normally, the tubes are not felt but the ovary may be felt in a thin patient. For every organ or structure palpated in the pelvis – including uterus and cervix – we should report on its site (position), size, shape, surface, consistency, mobility, tenderness, and relation to surrounding structures.
- d. **Speculum examination.** To inspect the cervix and vaginal walls using the Cusco self-retaining vaginal speculum.
- e. **In case of prolapse.** The tone of levator ani muscles is determined by placing two fingers in the vagina and the thumb on the perineum and the patient is asked to cough.
- f. **Rectal examination.** It is performed in certain cases: (i) to examine a virgin; (ii) to diagnose a rectocele or enterocele; (iii) to detect infiltration of uterosacral ligaments in case of cancer of cervix or body. These ligaments are better felt per rectum; (iv) for diagnosis of a mass in Douglas pouch; (v) to examine a rectovaginal fistula and complete perineal tear; (vi) the presence of rectal symptoms as bleeding.

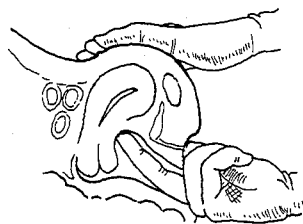


Fig.18. Bimanual examination

Note. The patient should empty the bladder before examination otherwise the uterus will be difficult to define. An exception to the above is when the patient complains of stress incontinence.

C. SPECIAL INVESTIGATIONS

These, vary according to the lesion present. There are noninvasive and invasive methods of investigation.

- a. **Noninvasive investigations.** Cytology, microbiology, hormonal assay, sonography, radiology, computed tomography (CT scan), magnetic resonance imaging, colposcopy and colpomicroscopy.
- b. **Invasive investigations.** Dilatation and curettage, biopsy from suspected lesions, hysterosalpingography, hysteroscopy, laparoscopy and laparotomy.

Note. Culdoscopy has been replaced by laparoscopy.

SONOGRAPHY

INDICATIONS IN GYNAECOLOGY

- A) Diagnostic:** Gynaecologic ultrasound can be used for the diagnosis of: (1) Ovarian cyst or mass; (2) polycystic ovary syndrome; (3) corpus luteum cyst; (4) follicular growth. Ovulation is about to occur when the graafian follicle reaches a diameter of 18-24 mm. This is important in infertile patients to know the response to hormonal treatment and to choose the time of ovum collection for In Vitro Fertilization (IVF); (5) uterine fibroids, endometrial carcinoma, adenomyosis, and intrauterine adhesions; (6) uterine anomalies as bicornuate uterus; (7) missed intrauterine contraceptive device to locate its site; (8) pelvic mass to know its size, site, consistency and nature; (9) breast masses; (10) liver metastases and gallbladder disease; (11) renal abnormalities; (12) ascites; (13) tubal patency by sonohysterosalpingography.
- B) Invasive Procedures:** (1) Retrieval of ova for In Vitro Fertilization; (2) aspiration of simple ovarian cyst, endometriotic ovarian cyst, tubo-ovarian cyst and tubo-ovarian abscess; (3) treatment of intact tubal pregnancy by injecting methotrexate, prostaglandin, potassium chloride or hyperosmolar glucose solution into the intact pregnancy sac; (4) biopsy of recurrent pelvic masses in case of malignancy; (5) placement of intracavitary radium.

The basic principles of sonography and Doppler ultrasound are discussed in "**BASIC OBSTETRICS**".

SECTION III

MENSTRUAL DISORDERS

DYSMENORRHOEA

Dysmenorrhoea means pain related to menstruation.

TYPES

1. Spasmodic dysmenorrhoea.
2. Membranous dysmenorrhoea.
3. Congestive dysmenorrhoea.

SPASMODIC (PRIMARY, IDIOPATHIC) DYSMENORRHOEA

It is a common complaint in young girls (teenagers). Pain occurs in absence of any organic pelvic lesion.

Clinical Picture

Age

It usually starts 1 or 2 years after menarche because the first cycles are usually anovulatory. This dysmenorrhoea occurs only in ovulatory cycles and usually improves after the age of 25.

Parity

Pain improves or disappears after an abortion or labour because dilatation of the cervix causes laceration of the nerve fibres which transmit pain. Also pregnancy may complete the development of the myometrium and its blood supply.

Family History

There is increased incidence among mothers and sisters of women with primary dysmenorrhoea.

Type of Pain

Pain starts on the first day of menstruation, reaches its maximum within 24 hours while the bleeding is slight, and then improves when the flow becomes established. In few cases pain is felt through the whole period. Pain is colicky, intermittent, felt in the suprapubic region and is often referred to the inner and front sides of the thighs. Pain affects mainly the areas of the body supplied by the first lumbar nerve.

Associated Symptoms

Nausea, vomiting, diarrhoea, and urinary disturbances may accompany pain. These symptoms can be explained by entry of prostaglandin $F_{2\alpha}$ into the systemic circulation. In primary dysmenorrhoea there is increased production of this prostaglandin in the endometrium.

Aetiology

Spasmodic dysmenorrhoea is explained by more than one theory because not all cases arise in the same way.

a. Abnormal Anatomy

1. Cervical obstruction; due to cervical stenosis or retroflexion of the uterus. This causes retention of menstrual blood. The retained blood causes irregular and painful contractions. Also there may be increased reabsorption of prostaglandins from retained blood. At the same time blood may regurgitate along the tubes into the peritoneal cavity leading to peritoneal irritation and pelvic pain.
2. Uterine hypoplasia. The underdeveloped muscle is unable to expel the blood which accumulates causing dysmenorrhoea.

b. Abnormal Physiology

1. Low pain threshold.
2. Ischaemia of uterine muscle, resulting in pain similar to that of angina pectoris.
3. Hypersensitivity of the sympathetic nerve fibres of the uterus. This exaggerates the sensory impulses transmitted along them.
4. Disturbed polarity of the uterus. Uterine polarity means when the fundus contracts the cervix dilates and vice versa dilatation of cervix reflexly causes uterine contraction. The disturbed polarity leads to difficulty in discharge of menstrual blood resulting in pain.
5. Clotting of menstrual blood. The clots are difficult to expel, however, clots may be passed without causing pain.
6. Hormonal imbalance. Relative excess of progesterone causes contraction of the uterine isthmus and formation of a thick endometrium which is difficult to be expelled through the cervix. Anovulatory cycles are painless due to absence of progesterone.
7. Prostaglandin effect is the most accepted theory. In primary dysmenorrhoea there is increased production of prostaglandin $F_{2\alpha}$ in the endometrium. It causes vasoconstriction and uterine ischaemia which may cause the pain of dysmenorrhoea. It also causes strong uterine contractions (uterine spasm). Progesterone stimulates the production of prostaglandins in the endometrium and so anovulatory cycles are painless. The production of prostaglandins reaches a peak at, or soon after, the start of menstruation. With the onset of bleeding, the formed prostaglandins are released from the shedding endometrium.

PGF₂ α also causes contraction of the gut musculature leading to nausea, vomiting, and diarrhoea reported by many women.

c. General Causes

1. Psychological disturbances. Pain may be an excuse to avoid school, work, etc. The disorder is frequent in girls whose mothers had the same complaint.
2. Smoking. This may release prostaglandins within the uterus.

Treatment

1. General Treatment

(a) Explanation and reassurance of the patient; (b) avoid sedentary life and encourage muscular exercises; (c) treatment of constipation and restriction of coffee; (d) yoga and acupuncture may be tried.

2. Nonhormonal Treatment

(a) Antispasmodics; (b) analgesics; (c) antiprostaglandins which inhibit the synthesis of prostaglandins as naproxen or ibuprofen (Brufen tablets 400 mg thrice daily during the period). Pain is relieved in 80% of cases.

3. Hormonal Treatment

Indicated when medical treatment fails. The main idea is to inhibit ovulation because anovulatory cycles are painless. Hormonal treatment is given for 6-12 successive months.

- a. Combined contraceptive tablets to inhibit ovulation. Pain is relieved in 90% of cases.
- b. The dydrogesterone compound Duphaston does not inhibit ovulation but relieves pain by reducing the strength of uterine contractions. One tablet (10 mg) is given twice daily for 21 days starting on 5th day of the cycle.

4. Surgical Treatment

Indicated when hormonal treatment fails.

- a. Dilatation of the cervix. The cervix is dilated to 10 mm (No 10 Hegar dilator). Excessive dilatation may be associated with incompetent cervix in a subsequent pregnancy. This cures 60% and improves 20% of cases. Dilatation acts as a local sympathectomy by causing laceration of the nerve fibres around the internal os which transmit pain, and by stretching the fibromuscular tissue at the internal os rendering it hypotonic. Sometimes after a period of relief lasting 6 months to 2 years, pain recurs due to regeneration of the nerve fibres. Dilatation can be repeated.
- b. Presacral sympathectomy (neurectomy). Indicated when all other measures fail. It is an abdominal operation to remove the presacral nerve or plexus of nerves lying in front of the 4th, 5th lumbar vertebrae and sacral promontory. About 80% are cured. Failure to obtain cure in every case is due to incomplete removal of the nerve tissue. Operation is done by laparotomy or laparoscopy.

- c. Laser uterine nerve ablation (LUNA). Through laparoscopy, laser is used to divide the uterosacral ligaments containing the nerve supply of the uterus. It is done alternative to presacral neurectomy.

MEMBRANOUS DYSMENORRHOEA

It is a rare type of spasmodic dysmenorrhoea in which pain is very severe and is relieved after the passage of an endometrial cast during the third or fourth day of menstruation. Typically, the cast is triangular in shape but sometimes, it is passed in the form of 2 or more large fragments.

Treatment is like spasmodic dysmenorrhoea in addition to repeated curettage to remove the unhealthy endometrium.

CONGESTIVE (SECONDARY) DYSMENORRHOEA

Aetiology

Pain is due to pelvic congestion which is caused by:

1. Chronic pelvic infection as cervicitis, endometritis or salpingitis.
2. Pelvic tumours as fibroids or ovarian cyst.
3. Abnormal position of the uterus as retroversion or prolapse.
4. Simple pelvic congestion due to chronic constipation or coitus interruptus.
5. Pelvic congestion syndrome due to broad ligament varicocele.
6. Endometriosis and adenomyosis lead to a specific type of dysmenorrhoea.
7. Extragenital lesions as chronic appendicitis.

Clinical Picture

Age

It usually occurs after the age of 30.

Parity

More in parous women.

Type of Pain

Pain starts several days (3-5 days) before the period, increases gradually as menstruation approaches and is relieved by the onset of the flow due to diminution of pelvic congestion. In some cases the pain is felt through the whole period. The pain is a continuous dull ache felt in the lower abdomen and accompanied with backache.

Associated Symptoms

Menorrhagia, polymenorrhoea and increased normal vaginal discharge (leucorrhoea) may occur.

Treatment

(1) Treatment of the cause; (2) analgesics; (3) measures to relieve pelvic congestion as ichthol in glycerine vaginal pessaries, warm vaginal douches and treatment of constipation. Ichthol is soothing for pain, and glycerine is hygroscopic and relieves congestion.

MITTELSCHMERZ OR OVULATION PAIN

CLINICAL PICTURE

It is a midcycle dull aching pain felt in one or other iliac fossa about the time of ovulation. It lasts for a few hours rarely longer than 24 hours. Sometimes accompanied with nausea and vomiting. Pain may be severe and mistaken for appendicitis or acute abdominal conditions. Occasionally it is accompanied by increased vaginal discharge or slight vaginal bleeding (ovulation bleeding) which is due to a fall in the level of oestrogen at the time of ovulation.

AETIOLOGY

The pain may be due to:

1. Increased tension within the ovary due to a thickened tunica albuginea which interferes with rupture of the graafian follicle at the time of ovulation (preovulatory).
2. Peritonism. Irritation of the peritoneum by fluid or blood from the ruptured follicle (ovulatory).
3. Tubal contractions. The tube shows active contractions at the time of ovulation (prostaglandin effect) which may cause pain (postovulatory).

TREATMENT

(1) Explanation and reassurance; (2) analgesics; (3) temporary inhibition of ovulation by contraceptive tablets given for 3 months. Spontaneous cure is always liable to occur.

PREMENSTRUAL SYNDROME (OVARIAN CYCLE SYNDROME)

DEFINITION

PMS means cyclic recurrence of psychological, behavioural, or somatic symptoms during the luteal phase of the menstrual cycle and in absence of organic disease. The symptoms are relieved by the end of menstruation. Symptoms occur only in ovulatory cycles. Symptoms must be severe enough to interfere with the woman's normal activities, and this differentiates PMS from premenstrual molimina.

PREVALENCE

It varies between 10 and 90%, however, severe PMS occurs in less than 10% of cases. This wide range of incidence is explained by the fact that more than 150 symptoms have been associated with PMS.

AGE INCIDENCE

It mostly occurs in women in their thirtieth and fortieth.

AETIOLOGY

The actual cause is unknown and the syndrome may be attributed to:

1. Endocrine Theory

- a. High oestrogen levels, or low progesterone levels, i.e., high oestrogen-progesterone ratio. Progesterone stimulates sodium loss thus preventing water retention, and has a sedative effect on the central nervous system.
- b. Allergic reaction to the corpus luteum so the syndrome is seen only with ovulatory cycles.
- c. Increased secretion of aldosterone which leads to salt and water retention.
- d. Increased antidiuretic hormone leading to water retention.
- e. Elevated serum prolactin.

2. Diet Theory

High intake of salt leading to water retention, low intake of refined sugar leading to hypoglycaemia, and magnesium deficiency.

3. Vitamin Theory

Deficiency of vitamin A, B₆, and E. Vitamin B₆ is a co-factor in the production of serotonin and dopamine.

4. Prostaglandin Theory

There is increased prostaglandin activity. Prostaglandins are produced in the brain, breast, gastrointestinal tract, kidney, and genital tract. These areas often present with symptoms in patients with PMS.

5. Endorphin Theory

There is a decrease in the level of beta-endorphins in the luteal phase. These endogenous opiates are associated with a sense of well-being. PMS symptoms mimic some symptoms of opiate withdrawal.

6. Serotonin Theory

Low serotonin level is associated with depression, while serotonin excess is associated with anxiety.

7. Psychological Disturbances

SYMPTOMS

1. Nervous symptoms: headache, migraine, palpitation, irritability, depression, insomnia, crying, and change in libido.
2. Behavioural symptoms as poor concentration, loss of motor skill, bad performance, hostility, and suicide attempts.

3. Gastrointestinal symptoms; as nausea, vomiting, diarrhoea, or constipation.
4. Mastalgia which means swelling and pain of the breasts.
5. Water retention manifested by oedema of the face, eyelids, and legs, and temporary increase in body weight.
6. Hypoglycaemia-like symptoms; as increased appetite, craving for sweets, and fatigue.
7. Pain in the form of backache and cramps.
8. Worsening of medical conditions as asthma, epilepsy, migraine, and rheumatoid arthritis.

DIAGNOSIS

It depends on the presence of symptoms which are related to the luteal phase of the cycle. Symptoms must be absent during the follicular phase. Physical examination and laboratory tests do not show abnormal findings. However, a complete physical examination must be done to exclude an organic cause that might be responsible for the symptoms.

TREATMENT

1. Explanation and reassurance.
2. Moderate exercise may be helpful by increasing production of endogenous endorphins.
3. Diet. Increase the carbohydrate intake by giving refined sugar to prevent hypoglycaemia-like symptoms and give primrose oil. Restriction of salt for 7-10 days premenstrually to reduce fluid retention. Reduce caffeine intake.
4. Diuretics. Given for symptoms of water retention. Spironolactone (Aldactone) is the diuretic of choice (100 mg daily). It inhibits aldosterone secretion.
5. Symptomatic treatment. Tranquilizers for irritability and antidepressants as fluoxetine (Prozac - 20 mg daily).
6. Progestogens. To improve luteal phase deficiency. Progesterone suppositories are inserted vaginally or rectally; 200-400 mg twice daily, or a progestogen oral tablet as norethisterone (Primolut-N) is given.
7. Dopamine agonists. Bromocriptine (Parlodel) or lisuride (Dopergin) tablets to inhibit prolactin secretion. It is tried if the main complaint is mastalgia. The dose of bromocriptine is one tablet (2.5 mg) twice daily.
8. Vitamin B₆ (pyridoxine). It increases the synthesis of dopamine which is the prolactin-inhibiting hormone (100 mg daily). It also increases the synthesis of serotonin.
9. Anti-prostaglandins. Effective in patients with headache, backache, cramps and mastalgia.
10. Danazol. It relieves mastalgia. It is considered only when other drugs have failed because it has many side effects.

Generally, the drugs are started 10-14 days before the period. Sometimes a combination of therapy is useful.

11. Inhibition of ovulation. This is the most appropriate treatment and is achieved by:
 - a. Combined oral contraceptives.
 - b. Oestradiol implants.

- c. Oestradiol skin patches.
 - d. Depo-Provera (medroxyprogesterone acetate) 150 mg IM every 3 months.
 - e. Gonadotrophin releasing hormone analogues (agonists). These lead to amenorrhoea, anovulation, and drop in oestrogen level (medical oophorectomy).
 - f. Mifepristone. It blocks ovulation and reduces the symptoms.
12. Psychotherapy for resistant cases.

AMENORRHOEA

Amenorrhoea means absence of menstruation.

TYPES

1. Primary amenorrhoea means failure of menstruation to occur by the age of 14 years in the absence of the secondary sex characters, or by the age of 16 years in the presence of secondary sex characters. The incidence is <1%.
2. Secondary amenorrhoea means cessation of menstruation for 3 months, if previous menses were regular, and for 6 months, if previous menses were infrequent. The incidence is 0.7%.

Note. Delayed menarche means spontaneous onset of menses in a woman older than 16 years who has no reproductive abnormalities.

AETIOLOGY

Amenorrhoea may be physiological or pathological.

Causes of Physiological Amenorrhoea

1. Before puberty due to a low secretion of gonadotrophin releasing hormone (GnRH).
2. After menopause due to disappearance of all ovarian follicles, so the ovaries will not respond to the pituitary gonadotrophins.
3. During pregnancy because of continuous production of large amounts of oestrogen and progesterone without withdrawal. Pregnancy is the commonest cause of secondary amenorrhoea.
4. Lactation. Prolactin inhibits the production of gonadotrophin releasing hormone and renders the ovary refractory to the action of pituitary gonadotrophins. It also inhibits ovarian steroidogenesis.
5. Periods of amenorrhoea may occur shortly after menarche due to immaturity of the hypothalamic-pituitary-ovarian axis or before menopause due to decreased number of ovarian follicles and their increased resistance to gonadotrophin stimulation.

Pathological Amenorrhoea

This may be false or true.

False Amenorrhoea "Cryptomenorrhoea"

In this condition, menstruation occurs but the blood is unable to escape due to the presence of obstruction in the genital tract as cervical stenosis, transverse vaginal septum, vaginal aplasia, and imperforate hymen. Cervical stenosis may be congenital or acquired after amputation or cauterization of the cervix.

Aetiology of True Pathological Amenorrhoea

I. General Causes

(1) Malnutrition; (2) voluntary weight loss (dieting); (3) obesity; (4) any acute illness can cause a short period of amenorrhoea; (5) chronic diseases as diabetes mellitus, pulmonary tuberculosis and chronic nephritis; (6) drugs as androgen and contraceptive pills; (7) hypercarotinaemia may cause amenorrhoea, cause is unknown. The ovaries are stained with the yellow carotene pigment (golden ovaries). Other tissues as the skin may be stained yellow; (8) jogger's amenorrhoea, seen frequently in women training for marathon racing and other forms of violent exercises. There is increased secretion of beta-endorphins and prolactin which inhibit the pulsatile release of GnRH.

Note. A certain amount of body fat is needed to have normal regular menstruation (Frisch theory). Suboptimal and supraoptimal amount of fat may impair oestrogen metabolism and leads to amenorrhoea. The weight usually needs to be more than 45 kg for menstruation to occur.

II. Hypothalamic Amenorrhoea

1. Organic lesions; traumatic, inflammatory as meningitis and encephalitis, or neoplastic.
2. Psychological disturbances as marked sorrow, war amenorrhoea, and change of environment.
3. False pregnancy "pseudocyesis". See Obstetrics.
4. Anorexia nervosa.
5. Bulimia.
6. Frolich syndrome.
7. Laurence-Moon-Biedl syndrome.
8. Isolated gonadotrophin releasing hormone deficiency and Kallmann syndrome.
9. Mental disorders as schizophrenia.
10. Electroconvulsive therapy.
11. Drugs as phenothiazines and methyl dopa (Aldomet) lead to hyperprolactinaemia and amenorrhoea. These drugs inhibit the secretion of dopamine.
12. Postpill amenorrhoea.
13. Functional hypothalamic amenorrhoea. It is supposed to be due to absence or reduced frequency of GnRH pulse leading to decreased production of FSH and LH. However, we cannot test the hypothalamus to prove this diagnosis which is made after excluding all other causes of amenorrhoea.



Note. Dopamine is the prolactin-inhibiting hormone or factor (PIH or PIF). Decreased secretion leads to hyperprolactinaemia.

III. Pituitary Amenorrhoea

1. Pituitary infantilism (Lorain syndrome).
2. Pituitary cachexia known as Simmonds disease or Sheehan syndrome.
3. Pituitary tumours: basophil adenoma leading to Cushing disease, acidophil adenoma leading to gigantism or acromegaly, and prolactinoma.
4. Craniopharyngioma. It arises from Rathke pouch. It causes pressure atrophy of the gonadotrophin secreting cells.
5. The empty sella syndrome.

IV. Disorders of the Thyroid Gland

Hypo- or hyperthyroidism may cause menstrual abnormalities including amenorrhoea. The mechanism of which is not clear.

V. Disorders of the Adrenal Glands

1. Hypofunction or Addison disease.
2. Hyperfunction due to hyperplasia, adenoma or carcinoma as in Cushing syndrome and congenital adrenal hyperplasia.

VI. Ovarian Amenorrhoea

(1) Gonadal dysgenesis including Turner syndrome; (2) the polycystic ovary syndrome; (3) destruction of both ovaries by radium, deep x-ray, chemotherapy, tuberculosis or carcinoma; (4) surgical removal of both ovaries; (5) virilizing ovarian tumours as androblastoma; (6) metropathia haemorrhagica; (7) persistent corpus luteum (Halban disease); (8) premature ovarian failure; (9) resistant ovary syndrome.

VII. Uterine Amenorrhoea

1. Absence of uterus; congenital or surgical removal.
2. Severe degree of hypoplasia.
3. Overcurettage removing the basal layer of endometrium.
4. Destruction of the endometrium by radium, tuberculosis, gangrenous endometritis occurring after abortion or labour.
5. Asherman syndrome or intrauterine adhesions occurring after curettage or infection (amenorrhoea traumatica).

VIII. Chromosomal Causes

As Turner syndrome (45 XO), superfemale (47 XXX) and testicular feminization (46 XY).

IX. Idiopathic Amenorrhoea. No cause can be detected.

DIAGNOSIS OF AMENORRHOEA

A. History

1. Personal history. (a) Age of the patient to exclude menopause; (b) marital state to exclude pregnancy.
2. Menstrual history. To know the type of amenorrhoea whether primary or secondary and its duration.
3. Obstetric history particularly for Sheehan syndrome.
4. Past history of chronic diseases as diabetes mellitus and tuberculosis, of operation on the genital tract as curettage, irradiation and previous intake of drugs and contraceptive tablets.
5. Family history of diabetes mellitus, tuberculosis, testicular feminization and polycystic ovary syndrome.
6. Present history. The presence of other symptoms as obesity, wasting, anosmia, galactorrhoea, psychological disturbances and hot flushes indicating premature menopause. Symptoms suggestive of pregnancy.

B. General Examination

1. Absence of secondary sex characters (breast development, axillary and pubic hair).
2. Signs of anaemia and general disease as tuberculosis.
3. Presence of hirsutism or virilization.
4. The presence of obesity or wasting. The body mass index is calculated.
5. The height, weight, and span are determined.
6. Examination of the thyroid, chest, and breasts and galactorrhoea is excluded by squeezing all quadrants of both breasts.
7. Examination of urine for sugar, protein and casts (for diabetes mellitus and chronic renal disease).

C. Abdominal Examination

For a pelvi-abdominal mass as pregnancy or haematocolpos.

D. Local Examination

To know the condition of vulva, clitoris, vagina, cervix, uterus, ovaries and the presence of pelvic masses.

E. Special Investigations

If the history and clinical examination do not reveal a cause the following tests are carried out as a routine: (a) progestogen challenge test; (b) estimation of serum FSH, LH, TSH, and prolactin. Hyperprolactinaemia is responsible for 20% of cases of secondary amenorrhoea.

Progestogen Challenge Test

Progesterone causes uterine bleeding if the endometrium has been primed with oestrogen. A progestogen as norethisterone, 5 mg tablet is given twice daily for five days. If withdrawal bleeding occurs (within 2 weeks usually after 2 to 7 days) it means that the ovary is producing oestrogen alone but not progesterone i.e. anovulation. If no bleeding occurs it means either the ovary is not producing oestrogen or the uterus is not responding as in case of intrauterine adhesions. In this case an oestrogen-progestogen challenge test is carried out. A combined oral contraceptive pill is given for three weeks. If no bleeding occurs this means a uterine cause of amenorrhoea. However, if bleeding occurs the fault is in the ovary and this ovarian failure may be primary in the ovary or secondary to pituitary failure.

Serum FSH and LH

(a) A high serum level of FSH (above 40 mIU/ml) indicates ovarian failure and that the ovary is not producing oestrogen; (b) low serum FSH (less than 5 mIU/ml) indicates a hypothalamic or pituitary problem; (c) an LH:FSH ratio 2 or more is diagnostic of polycystic ovarian disease.

Other investigations are done according to the history and clinical examination and include:

1. Investigations for uterine amenorrhoea:
 - Pregnancy test if pregnancy is suspected.
 - A uterine sound is passed to diagnose uterine hypoplasia.
 - Ultrasonography diagnoses uterine hypoplasia and Asherman syndrome.
 - Hystero-grography or hysteroscopy diagnoses Asherman syndrome.
 - Uterine curettage to diagnose tuberculous endometritis.
2. Investigations for ovarian amenorrhoea:
 - Ultrasonography diagnoses polycystic ovaries, streak gonads or a small ovarian tumour.
 - Laparoscopy may show a small ovarian tumour, streak gonads or polycystic ovaries.
3. Investigations for the adrenal glands:
 - Estimation of serum cortisol and ACTH to diagnose Cushing syndrome.
 - Serum 17 α -hydroxyprogesterone to diagnose congenital adrenal hyperplasia.
 - Computed tomography (CT) scan or magnetic resonance imaging (MRI) to exclude adrenal tumour.
4. Thyroid function tests for thyroid disorders.
5. Investigations for pituitary amenorrhoea:

If a pituitary tumour is suspected, we examine the retina and visual fields and do a CT scan or MRI which is more accurate but more expensive.
6. Glucose tolerance test if we suspect diabetes mellitus.

7. Chromosomal study must be done in every case of primary amenorrhoea as about 40% of these cases show chromosomal anomalies.

TREATMENT OF AMENORRHOEA

1. General Treatment

- (a) Proper diet, correction of malnutrition and obese patients are advised to lose weight;
- (b) psychotherapy if necessary.

2. Treatment of the Cause

Examples include control of diabetes mellitus, treatment of tuberculosis, and removal of a virilizing ovarian tumour. Hyperprolactinaemia is treated by a dopamine agonist as bromocriptine (Parlodel) or lisuride (Dopergin). Hypothyroidism is treated by thyroxine.

3. Hormonal Treatment

It is indicated in absence of an organic cause i.e. dysfunctional amenorrhoea.

- a. Cyclical treatment with oestrogen followed by progestogen like the normal cycle. The treatment is given for 3 successive months. This may be followed by restoration of normal cycles.
- b. Induction of ovulation. Clomiphene (Clomid) and gonadotrophins are only used if the patient is complaining of infertility. These drugs cause ovulation and menstruation. The gonadotrophin releasing hormone given intravenously or subcutaneously in a pulsatile fashion every 60-90 minutes using a computerized pump, can cause ovulation and menstruation if there is a hypothalamic dysfunction.

PRIMARY AMENORRHOEA

Aetiology

A. False amenorrhoea or cryptomenorrhoea. Due to congenital cervical stenosis, transverse vaginal septum, vaginal aplasia or imperforate hymen.

B. True amenorrhoea. The causes are:

I. Hypothalamic amenorrhoea:

- (1) Organic lesions; traumatic, inflammatory or neoplastic; (2) Frolich syndrome; (3) Laurence-Moon-Biedl syndrome; (4) isolated gonadotrophin-releasing hormone deficiency and Kallmann syndrome.

II. Pituitary amenorrhoea:

- (1) Pituitary infantilism (Lorain syndrome); (2) gigantism due to acidophil adenoma; (3) empty sella syndrome.

III. Hypothyroidism.

IV. Disorders of the adrenal glands:

- (1) Addison disease occurring in a young girl; (2) congenital adrenal hyperplasia.

V. Ovarian amenorrhoea:

(1) Gonadal dysgenesis including Turner syndrome and pure gonadal dysgenesis; (2) the polycystic ovary syndrome may present with primary amenorrhoea.

VI. Uterine amenorrhoea:

(1) Congenital absence as in Mayer-Rokitansky-Kuster-Hauser syndrome; (2) severe degree of hypoplasia.

VII. Hyperprolactinaemia.

VIII. Chromosomal causes:

These are responsible for about 40% of cases of primary amenorrhoea and include gonadal dysgenesis, superfemale, and testicular feminization. Gonadal dysgenesis is the commonest cause of primary amenorrhoea and accounts for about 30% of all cases.

IX. True hermaphrodite.

Note. The most common cause of primary amenorrhoea is constitutional delay, so the ages of menarche of the mother and any sister should be determined.

OLIGO- AND HYPOMENORRHOEA

Oligomenorrhoea means infrequent menstruation, so the length of the cycle is more than 35 days.

Hypomenorrhoea means scanty menstruation (less than 30 ml) or the duration of the flow is less than 2 days.

Oligo- and hypomenorrhoea often occur together.

Note. Absence of menstruation for 3 months or more is considered amenorrhoea and not oligomenorrhoea.

Aetiology

1. Constitutional oligohypomenorrhoea. It is present from the menarche. The patient is normal, the cycles are ovulatory and it requires no treatment.
2. Pathological type. The aetiology and treatment are like that of amenorrhoea.

SYNDROMES ASSOCIATED WITH AMENORRHOEA

Frolich Syndrome

It is a hypothalamic disturbance occurring from childhood. There is obesity, infantile genital organs, primary amenorrhoea, and sleepiness. The Laurence-Moon-Biedl syndrome has similar features but in addition there is retinitis pigmentosa, mental deficiency and polydactyly. Obesity affects the shoulder girdle, the breasts, the pelvic girdle and thighs.

Anorexia Nervosa

It is due to psychological disturbance affecting the hypothalamus and appetite. There is amenorrhoea, emaciation, weakness, hypoglycaemia, low basal metabolic rate and subnormal

temperature. FSH, LH, oestrogen, T_3 and T_4 are low. Treatment by psychotherapy. Ovulation induction is possible with clomiphene and pulsatile GnRH in patients wishing to conceive.

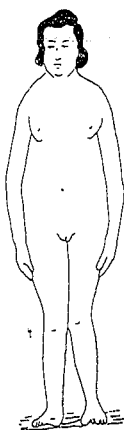


Fig.19. Frolich syndrome

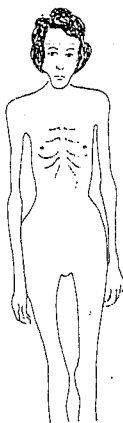


Fig.20. Anorexia nervosa



Fig.21. Cushing syndrome

Bulimia

The syndrome is marked by episodes of overeating followed by self-induced vomiting, fasting, or the use of laxatives and diuretics to avoid gain in weight. The patient usually has depressive symptoms with menstrual irregularities and amenorrhoea of hypothalamic origin. However, the patient may not develop amenorrhoea. Treated by behavioural therapy.

Kallmann Syndrome

Anosmia or hyposmia, infantile genital organs, and primary amenorrhoea due to isolated deficiency of GnRH. Sometimes this isolated deficiency is associated with other congenital abnormalities as colour blindness. Treatment is by cyclic oestrogen and progestogen to stimulate growth of the breasts, to induce menstruation, and to prevent osteoporosis.

Postpill Amenorrhoea (Shearman Syndrome)

Oral contraceptives inhibit ovulation by inhibiting the hypothalamic-pituitary axis leading to suppression of FSH and LH. Occasionally this suppression persists for several months after stopping the oral contraceptive producing postpill amenorrhoea. This occurs in less than 1% of cases, and is not related to the length of intake of the pill. This suppression resolves spontaneously and does not last more than 6 months. So if amenorrhoea lasts more than 6 months the case is investigated to determine the cause.

Pituitary Infantilism of Lorain

The physical and sexual development are arrested so there is dwarfism and hypogonadism. Only the production of the growth hormone and gonadotrophins is affected. The cause is unknown.

Pituitary Cachexia (Panhypopituitarism)

In Simmonds disease there is destruction of the anterior lobe of pituitary due to any cause in either sex e.g. septic embolic due to postpartum infection. In Sheehan syndrome there is spasm and thrombosis of the anterior pituitary arterioles due to severe postpartum haemorrhage, so it occurs only in females. This leads to hypogonadism, hypothyroidism, and adrenocortical insufficiency, so there is atrophy of the breasts and genital organs, amenorrhoea and failure of lactation (deficiency of prolactin) after delivery. Absence of lactation is the first sign. Other manifestations include falling of hair, hypotension, hypoglycaemia, weakness and loss of weight with pale waxy skin (deficiency of melanocyte stimulating hormone). More than 75% of the anterior pituitary has to be destroyed to produce symptoms of deficiency. Treatment by cortisone and thyroxine for life. Oestrogen-progestogen therapy is given to induce menstruation. If pregnancy is desired we give gonadotrophins.

Note. The posterior lobe of the pituitary gland is not affected by severe postpartum haemorrhage as blood is shifted from the anterior lobe to the posterior lobe during labour as the latter is active and secretes oxytocin and so it is not affected by ischaemia.

The Empty Sella Syndrome

It is a congenital condition due to herniation of the subarachnoid space into the sella turcica (pituitary fossa). The syndrome can also occur secondary to surgery, radiotherapy or infarction of a pituitary tumour. The hernial sac containing cerebrospinal fluid will lead to compression of the pituitary gland and enlargement of the fossa. It may lead to amenorrhoea and is sometimes associated with hyperprolactinaemia. It is diagnosed only by CT or MRI which is more accurate.

Cushing Syndrome

The clinical picture is due to hyperfunction of the adrenal cortex. It is characterized by amenorrhoea, hirsutism, acne, trunkal obesity, muscle wasting and weakness, moon face, striae of the skin, hypertension, hyperglycaemia, osteoporosis, and polycythemia.

Actiology

1. Pituitary Cushing syndrome; due to basophil adenoma leading to over production of ACTH and subsequent bilateral adrenal hyperplasia. Usually called Cushing disease. Treated by trans-sphenoidal removal of the tumour and/or deep x-ray therapy.
2. Adrenal Cushing syndrome; due to adenoma or carcinoma of the adrenal gland. Excessive production of cortisol results in complete suppression of ACTH secretion and atrophy of the contralateral adrenal gland. The lesion is usually bilateral. Treatment is bilateral adrenalectomy and cortisol for life.
3. Hypothalamic Cushing syndrome. There is excessive production of ACTH in absence of pituitary tumour. The disorder is in the hypothalamus.
4. Ectopic Cushing syndrome. Some malignant tumours as lung cancer may produce ACTH.

Note. The adrenal cortex produces corticosteroids, mineralosteroids, and sex hormones (androgen and oestrogen).

Congenital Adrenal Hyperplasia. See intersex.

Gonadal Dysgenesis

It means failure of the gonad to develop and will be in the form of fibrous bands "streak gonads." Two syndromes are described.

1. Turner Syndrome

This is the commonest type of gonadal dysgenesis. The chromosomal arrangement is 45XO or mosaic 45XO-46XX, or 45XO-46XY. Turner syndrome is characterized by physical abnormalities, so the patient is short (<150 cm) with webbing of the neck (50%), shielding of the chest, coarctation of the aorta, cardiac and renal abnormalities, cubitus valgus, deformities of the ears, fingers, and toes. The breasts remain underdeveloped with widely spaced nipples, and the genital organs are infantile. The ovaries are in the form of fibrous bands with no follicles i.e.

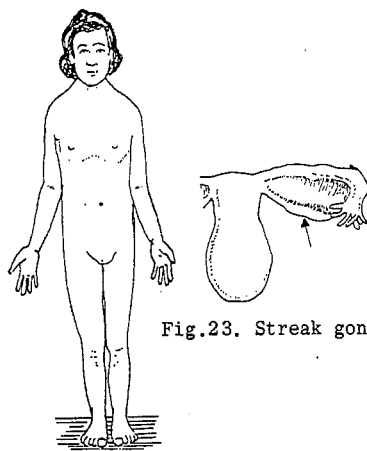


Fig.23. Streak gonads

Fig.22. Turner syndrome

streak gonads. There is primary amenorrhoea. Because the ovaries are inactive the oestrogen level is low and FSH and LH levels are high (hypogonadotropic hypogonadism). Treatment is by cyclic oestrogen and progestogen to stimulate growth of the breasts, to induce menstruation and to prevent osteoporosis. Oestrogen is not given alone as it may cause endometrial carcinoma. We can give conjugated oestrogens (Premarin), 0.625 mg daily and medroxyprogesterone acetate (Provera tablets), 5-10 mg daily for 10-14 days each month. Treatment is started when bone age is greater than 13 years to avoid early closure of bone epiphyses. To increase final height, growth hormone can be given before starting oestrogen therapy. It increases height by about 8 cm. If the karyotype is mosaic with Y chromosome, the streak gonads are testicles and should be removed as early as possible, as the risk of malignancy is high about 25%, because the gonad is abnormal in structure. Pregnancy can be achieved in Turner syndrome using donated oocytes (condemned in Moslem countries).

Notes for the postgraduate

1. Loss of genes on the short arm of one X chromosome leads to the short stature and physical abnormalities of Turner syndrome. Loss of genes on the long arm of one X chromosome leads to streak gonads and primary amenorrhoea.
2. Some mosaic cases of Turner syndrome with karyotype 45XO-46XX have functioning ovaries due to the presence of normal cells (46XX). These patients may appear as normal females. On

rare occasions they menstruate and may even become pregnant. However, they are liable to have premature ovarian failure leading to premature menopause.

3. Bone age is determined by x-ray examination of the hand and wrist and compared with a standard for patient age. The nondominant hand is used for x-ray examination.
4. Noonan (or Ulrich) syndrome. Affects males and females. Normal chromosomes, normal gonads but with physical abnormalities of Turner syndrome. The patient is fertile.
5. Turner syndrome is the commonest chromosomal abnormality occurring in females. It has increased incidence of hypertension, diabetes, deafness, and colour blindness (red and green).

2. Pure Gonadal Dysgenesis

The patient has streak gonads, infantile breasts and genital organs, and primary amenorrhoea. She is often taller than normal and does not show the physical abnormalities of Turner syndrome. The karyotype is 46XX or 46XY. When the karyotype is 46 XY, the condition is termed Swyer syndrome. Treated in the same way as Turner syndrome.

Polycystic Ovary Syndrome (PCOS)

The syndrome was first described by Stein and Leventhal in 1935, and the old name was Stein-Leventhal syndrome.

Prevalence

About 5-10% of women in the reproductive age have PCOS.

Aetiology

The syndrome is due to hyperandrogenism which is due to one or more of the following factors:

1. Hypothalamic and/or pituitary abnormality in the form of increased LH secretion. LH stimulates the theca cells of the ovary to produce androgens.
2. Genetic deficiency of the aromatase enzyme which is necessary for the conversion of ovarian androgens to oestrogens. Some patients – but not all – show familial tendency to develop the syndrome (mother or sister). In fact about 50% of first degree relatives have PCOS.
3. Hyperinsulinaemia, due to increased peripheral resistance to insulin. It is present in about 50% of cases, and affects both obese and nonobese patients. It leads to hyperandrogenism which is explained by: (a) decrease in the hepatic synthesis of sex-hormone binding globulin, and this increases free testosterone, and free oestradiol; (b) inhibition of hepatic synthesis of insulin growth factor-1 (IGF-1) binding globulin leading to increased free IGF-1. This factor increases the sensitivity of theca cells in the ovary to the action of LH; (c) increased production of IGF-1 in the ovary; (d) increased secretion of dehydroepiandrosterone sulphate (DHEAS) from the suprarenal gland.
4. Suprarenal abnormality may lead to overproduction of suprarenal androgens.

In fact, the excess androgens come from the ovaries or from the ovaries and suprarenal glands.

Clinical Picture

Most cases occur between the ages of 17 and 30 years. Patient complains of one or more of the following:

1. Menstrual abnormalities in the form of primary or secondary amenorrhoea, oligomenorrhoea, occasionally menorrhagia, or irregular uterine bleeding. In many patients, the menstrual disturbance dates from menarche. It is the commonest presenting feature (80%).
2. Infertility due to anovulation.
3. Obesity in about 50% of patients.
4. Hirsutism in 60-80% of patients in USA and in 10-20% of Japanese patients.
5. Male alopecia and acne vulgaris.
6. Acanthosis nigricans. It is a gray-brown discoloration of the skin usually affecting the neck, axillae, under the breasts, groin, and vulva. It is due to hyperinsulinaemia.

Pathology

1. Ovaries. Both ovaries are enlarged 2-3 times the normal size and are cystic. The tunica albuginea is thick, smooth, white, and does not show the indentations of the normal ovary (porcelain ovaries or ping-pong ball appearance). There is no ovulation as the follicles do not rupture and become cystic. There are multiple small subcapsular cystic follicles (microcysts) which are filled with clear fluid rich in androgens. There is hyperplasia of the theca interna cells around the cystic follicles. This hyperthecosis is due to increased secretion of luteinizing hormone (LH) and the cells are often luteinized. The metabolism in the ovary is disturbed with increased production of androgens in the form of testosterone, androstenedione, and dehydroepiandrosterone (DHEA).
2. Endometrium. It is proliferative or hyperplastic due to unopposed oestrogen (anovulation and absence of progesterone). It may be atrophic due to excess androgens.

Hormonal Profile

(1) Increased LH in about 40% of cases; (2) normal or low FSH; (3) increased LH:FSH ratio to be 2 or more; (4) increased oestrone and free oestradiol; (5) increased androgens: testosterone (in 70%), androstenedione (in 50%), and DHEA. Dehydroepiandrosterone sulphate (DHEAS) which comes from adrenal glands (almost 100%) is raised in about 50% of cases; (6) fasting serum insulin is increased in about 50% of cases.

The serum FSH and LH are measured on day 2, 3, or 4 of the menstrual cycle to have a basal secretion of both hormones. At this time, LH is considered high if it is >10 mIU/ml and FSH is considered normal if it is <10 mIU/ml.

Key Points

1. Oestrone is increased due to increased peripheral conversion of androstenedione into oestrone in body fat.

2. High oestrone level leads to increased secretion of LH and decreased that of FSH.
3. Increased LH secretion causes hyperplasia of the theca interna cells (hyperthecosis) and increased production of androgens.
4. Increased testosterone leads to thickening of the tunica albuginea and atresia of ovarian follicles.
5. Obesity reduces hepatic synthesis of sex-hormone binding globulin (SHBG) and increases free testosterone and free oestradiol.
6. Obesity and hyperandrogenism lead to increased insulin resistance.
7. There is relative excess of LH to FSH, and this leads to failure of ovulation. FSH is necessary for the development of the mature graafian follicle.
8. Ovarian androgens are secreted mainly from the theca interna cells, but also from ovarian stroma cells.

Diagnosis

1. Diagnosis is easily made by the clinical picture alone.
2. Hormonal profile.
3. Glucose tolerance test which is impaired in some cases, fasting serum insulin is measured to diagnose hyperinsulinaemia (normal 10-20 U/ml), and fasting glucose: fasting insulin ratio is determined to diagnose increased insulin resistance. A ratio less than 4.5 is abnormal and indicates increased insulin resistance.
4. Sonography. It shows the presence of 12 or more cystic follicles (microcysts) in each ovary and/or ovarian volume more than 10 cm³. The microcysts are 2 to 10 mm in diameter and are arranged either peripherally under the capsule giving a necklace-like appearance or they are scattered throughout the ovarian stroma. The increase in the stroma volume increases the production of androgens. Doppler ultrasound shows increased blood flow to the stroma.
5. Laparoscopy. When done in case of infertility it diagnoses the polycystic ovaries.

Note. 10-25% of normal women with regular cycles show polycystic ovaries without the clinical features of PCOS. Also about 15% of women on oral contraceptives show the ultrasound findings typical of PCOS.

Complications of PCOS

1. Menstrual abnormalities.
2. Infertility due to anovulation.
3. Hirsutism.
4. Increased risk of endometrial carcinoma due to anovulation and absence of progesterone resulting in unopposed oestrogen action. There is also increased risk of ovarian carcinoma.
5. Patient may develop type II diabetes mellitus due to increased insulin resistance.

6. Increased risk of hypertension and coronary heart disease. Both hyperinsulinaemia and hyperandrogenism increase the low-density lipoproteins and triglycerides and lower the high-density lipoproteins.
7. During pregnancy, there is increased incidence of abortion, and gestational diabetes.

Treatment

I. General Treatment

1. Obese women should lose weight. Obesity reduces SHBG and increases free testosterone. It leads to increased insulin resistance and hyperinsulinaemia. It also increases LH level by increasing peripheral oestrogen production. Loss of weight produces opposite effects.
2. Smoking is stopped as it may increase the adrenal androgens.

II. If the Patient Does Not Desire Pregnancy

1. A progestogen is given for 10 days each month to regulate the menstrual cycle and prevent endometrial hyperplasia resulting from unopposed oestrogen. Medroxyprogesterone acetate tablets (Provera tablets), 10 mg daily for 10 days each month.
2. The use of a combined oral contraceptive. It produces the above mentioned effects.
3. In case of hirsutism we give a combined oral contraceptive which has no or little androgenic effects as Diane tablets and the new contraceptive tablets containing third-generation progestogens, e.g. Marvelon or Gynera tablets. Other drugs are also used for treatment of hirsutism.

III. If the Patient Desires Pregnancy

The treatment will be medical, surgical, or assisted reproductive techniques.

1. Medical Treatment

The following drugs are used to induce ovulation:

- a. Clomiphene citrate (Clomid).

If clomiphene therapy fails to induce ovulation, one of the following is tried:

1. Clomiphene + human chorionic gonadotrophin (HCG).
2. Clomiphene + dexamethasone, if the patient is having a high level of dehydroepiandrosterone sulphate (DHEAS) which is secreted by the adrenal glands. Dexamethasone, 0.5 mg orally at bedtime to inhibit the ACTH peak which occurs during sleep.
3. Letrozole (Femara). The dose is 2.5 mg daily for 5 days starting on third day of cycle. When the ripe follicle reaches 18 mm or more in diameter HCG is given. The drug inhibits peripheral oestrogen production (aromatase inhibitor). This leads to increased FSH which is necessary for the development of the mature graafian follicle. The drug can be combined with clomiphene.
4. Gonadotrophins + HCG.
5. Gonadotrophin releasing hormone given in a pulsatile manner.



- b. Insulin sensitizing agents. Some oral hypoglycaemics can be given if there is hyperinsulinaemia. These drugs reduce insulin resistance, insulin secretion, and secretion of androgens. They can induce ovulation and lead to pregnancy. If treatment fails they are combined with clomiphene. The dose of metformin (Glucophage) is 500 mg 2 or 3 times daily, given for 6-12 months.

Note. Gonadotrophins include human menopausal gonadotrophins, urinary FSH, and recombinant FSH.

2. Surgical Treatment

Indicated when medical treatment fails to induce ovulation, and it may be done alternative to stimulation with gonadotrophins which carries the risk of ovarian hyperstimulation, multiple pregnancy and its complications, and the need for intensive monitoring of the patient during stimulation.

Surgical treatment is by ovarian drilling. Diathermy coagulation of the ovaries is done using the laparoscope. The strength of the current, time of application, and number of points to be cauterized are not standardized. Some use a current of 40 watts for 4 seconds to cauterize 4 points in each ovary. LASER may be used for ovarian drilling (YAG, carbon dioxide, or KTP LASER). The rate of ovulation is about 70-80%, and rate of pregnancy is about 40%. Complications of drilling include pelvic adhesions. Also destruction of ovarian tissue may be followed by premature ovarian failure and possible ovarian cancer.

Notes

- Wedge resection of both ovaries is no more done as it may be followed by periovarian and peritubal adhesions which prevent pregnancy.
- Drilling destroys ovarian stroma and so reduces androgen production.

3. Assisted Reproductive Techniques

Resorted to if all measures fail to achieve pregnancy. These include intrauterine insemination, in Vitro Fertilization and Embryo Transfer.

Note. The rate of abortion is high (25-40%) in women with PCO who become pregnant. This may be due to a high level of LH in the follicular phase. This leads to early meiosis and an aged oocyte (abnormal ovum). Also during pregnancy, there is increased incidence of gestational diabetes mellitus.

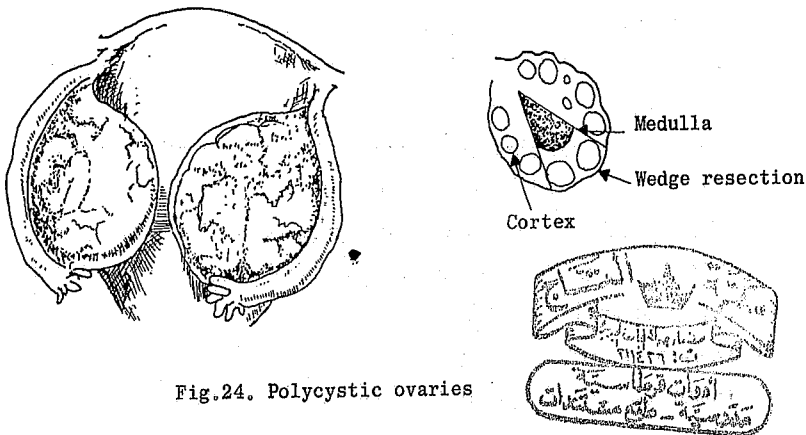


Fig.24. Polycystic ovaries

Resistant Ovary Syndrome (Savage Syndrome)

It is confined to women below 35 years of age. For some unknown reason the ovary fails to respond to pituitary gonadotrophins. This may be due to lack of sensitivity, absence, or decreased number of gonadotrophin receptors on the ovarian follicles. This leads to high levels of FSH and LH and low oestrogen level. The ovaries show normal number of follicles. The condition is only diagnosed by ovarian biopsy to differentiate it from premature ovarian failure. The biopsy should include the full thickness of the ovary as the normal follicles may be deeply located in the ovarian stroma. Some cases may recover spontaneously and get pregnant. Treatment is by repeated induction of menstruation with cyclic oestrogen-progestogen therapy and this may be followed by spontaneous recovery. If the patient wants to conceive, large doses of gonadotrophins are tried, however, the chance of pregnancy is very poor. Also ovum donation can be tried, however, this is condemned in Moslem countries.

Asherman Syndrome (Amenorrhoea Traumatica)

Aetiology

Intrauterine adhesions (IUA-synechiae) may occur as a result of:

1. Excessive uterine curettage after abortion (commonest cause), postpartum, diagnostic and therapeutic curettage.
2. Uterine infection; postabortive, postpartum, tuberculous, and bilharzial infection.
3. Myomectomy and caesarean section.
4. After insertion of intrauterine contraceptive device, and radium.

Classification of IUA by Hysteroscopic Findings

1. Minimal degree. Less than one-fourth of the uterine cavity involved by adhesions.
2. Moderate degree. One-fourth to three-fourths of uterine cavity involved by adhesions.
3. Severe degree. More than three-fourths of uterine cavity involved by adhesions.

Symptoms

Slight adhesions are not associated with symptoms. However, the patient may complain of hypomenorrhoea, amenorrhoea, dysmenorrhoea, and infertility (most common symptom). Hypomenorrhoea, and amenorrhoea are due to reduction in the surface area of the bleeding endometrium, as the endometrium is replaced by fibrous tissue. Infertility is due to mechanical obstruction in the cervical canal and uterine cavity preventing ascent of spermatozoa, or the poor decidual reaction in the endometrium interfering with implantation of the ovum. During pregnancy, the patient may complain of repeated abortion (lack of space in the uterine cavity), preterm labour, placenta praevia, and placenta accreta as the decidua basalis is absent or poorly formed due to over curettage.

Note. Obliteration of the region of the uterine isthmus by adhesions leads to reflex inhibition of the endometrium and amenorrhoea, but not cryptomenorrhoea.

Diagnosis

1. History of operation on the uterus or uterine infection.
2. In some cases the external os of the cervix is reduced to a very small hole or completely stenosed. If a uterine sound is passed it shows a limited mobility inside the uterus.
3. Negative progestogen and oestrogen-progestogen challenge tests in the presence of normal levels of FSH and LH (refractory endometrium).
4. Adhesions are seen by hystero-graphy (filling defects), sonography, or by hysteroscopy which is more accurate as it detects minimal adhesions which do not appear on hystero-gram.

Treatment

Adhesions are divided blindly by dilatation and curettage, or better under direct vision using the hysteroscope. In this case adhesions are divided by cutting, cautery, or lysed with laser. The uterine walls are kept apart by inserting an intrauterine contraceptive device as Lippes loop which is left for three months, or better by the use of a paediatric Foley catheter which balloon is filled with 3 ml sterile saline. The catheter is left for 7 days during which a broad-spectrum antibiotic is given. The patient must be treated for 3-6 months with high doses of oestrogen, e.g. conjugated oestrogens (Premarin) 2.5 mg orally daily for 3 weeks, adding medroxyprogesterone acetate tablets (Provera) 10 mg daily during the third week. The course is repeated after one week rest. Oestrogen helps regeneration of the endometrium. Treatment leads to pregnancy in 70-80% of cases. However, the rate of abortion may be higher than normal, and the risk of placenta accreta is increased.

The Superfemale or Triple X Syndrome

The individual is a female with 47 or 48 chromosomes (47XXX or 48XXXX). The genital organs are infantile with oligomenorrhoea, amenorrhoea, infertility, and mental deficiency. Gonadotrophins may be tried to induce ovulation and menstruation but the ovaries may be refractory. However, the majority of superfemales are normal in every way and fertile.

Testicular Feminization or Complete Androgen Insensitivity Syndrome

The patient is an attractive female with well-developed large breasts with small nipples and pale areola, smooth hairless skin and normal vulva. Pubic and axillary hair are absent or scanty. The fallopian tubes and uterus are absent or rudimentary. The lower part of the vagina which is developed from the urogenital sinus is present and so the vagina is short and blind but sometimes it is of normal length. The gonads are testes and found intra-abdominally or in



Fig.25: Testicular feminization

hernial sacs in the groins or upper labia. The karyotype is 46XY (male). The target organs (breasts, hair follicles, and vulva) are not sensitive to the androgens secreted by the testes due to absence of androgen receptors and so they develop in the female direction. There is often a positive family history. It is inherited as an X-linked recessive gene. The treatment is removal of the testes to avoid malignancy (5-25%) then oestrogen is given to avoid menopausal symptoms, osteoporosis, and to maintain the feminine characteristics. If the vagina is not adequate for coitus, gradual dilatation or plastic surgery is performed. The testes are removed after puberty (at 16-18 years) and when breast development is complete. If removed before puberty the breasts will not develop because the testes are the source of oestrogen.

Notes for the postgraduate

1. Testicular feminization was first described by Morris, so also known as Morris syndrome and androgen resistant (insensitive) syndrome.
2. Testicles do not show spermatogenesis.
3. Serum testosterone is in the normal male range (7.8 nanograms/ml).
4. The Sertoli cells of the testicle produce antimüllerian hormone which inhibits the development of the müllerian duct on the same side. This explains why the fallopian tubes and uterus are absent or rudimentary.
5. Absent uterus in a normal appearing female occurs only in 2 conditions: androgen insensitivity and müllerian agenesis.
6. Incomplete androgen insensitivity syndrome. The karyotype is 46XY, female features but with some pubic and axillary hair and enlarged clitoris.

The Galactorrhoea Amenorrhoea Syndrome

See hyperprolactinaemia.

HYPERPROLACTINAEMIA

Prolactin is a polypeptide hormone secreted by lactotrophs (lactotropes) which are derived from the chromophobe cells of the anterior pituitary gland. The prolactin-inhibiting hormone or factor (PIH or PIF) which is dopamine inhibits the secretion of prolactin. Oestrogens, serotonin, and thyrotrophin releasing hormone act directly on the lactotrophs and increase prolactin secretion. The normal serum level in the female is 2-20 nanograms/ml, or 40-400 mIU/ml. The main function of prolactin is production of milk from the mammary glands, i.e., lactation. Prolactin is present in 4 forms according to its molecular weight. Small prolactin with a low molecular weight, big prolactin, big-big prolactin and glycosylated prolactin. Small prolactin is the more bioactive form of the hormone, and 80% of prolactin is present in this small form. The other 3 forms have low bioactivity and this explains the occasional presence of hyperprolactinaemia in association with normal ovulatory cycles.

CAUSES OF HYPERPROLACTINAEMIA

1. Physiological

1. Pregnancy due to high oestrogen level.
2. Lactation. Suckling and breast stimulation lead to reflex suppression of PIH.
3. Stress. Any type of stress including exercise, vaginal examination, palpation of the breast and difficult venous puncture when the blood sample is taken.
4. Sexual intercourse
5. Sleep. Prolactin secretion increases during sleep. The highest secretion occurs between 5 and 7 AM.
6. Frequent nipple stimulation in search for galactorrhoea in obsessed women.
7. Hypoglycaemia.

2. Pathological

1. Hypothalamic disorders leading to decreased secretion of PIH.
 - a. Functional. There is hyperprolactinaemia in absence of a detectable cause, i.e., idiopathic hyperprolactinaemia.
 - b. Organic lesions due to trauma, infections (meningitis, encephalitis) and tumours.
 - c. Psychological disturbances as depressive psychosis.
2. Pituitary lesions: (a) Prolactin secreting tumours (prolactinomas); (b) empty sella syndrome; (c) growth hormone secreting tumour. Hyperprolactinaemia is present in about 30% of cases of acromegaly. It is due to compression of pituitary stalk by the tumour leading to deficiency of dopamine or the presence of a mixed growth hormone and prolactin secreting tumour. Pituitary adenoma is the commonest cause of hyperprolactinaemia and present in 40-50% of cases.
3. Primary hypothyroidism. The thyrotrophin releasing hormone is increased and stimulates the lactotrophs. It is responsible for 2-5% of cases.
4. Drugs. Account for 1-2% of cases and include many drugs as oestrogens, combined oral contraceptives, antihypertensives as methyl dopa (Aldomet) and reserpine, antihistaminics, antiemetics as metoclopramide (Primperan), tranquillizers, antidepressants, narcotics and phenothiazines. Drugs act by inhibiting the secretion of dopamine or block the dopamine receptors. Oestrogen directly stimulates the lactotrophs and also inhibits the secretion of dopamine.
5. Chronic liver disease. Prolactin is inactivated in the liver.
6. Chronic renal disease due to decreased excretion of prolactin.
7. Lung and renal tumours, uterine myoma, and other ectopic tumours may secrete prolactin.
8. Diseases of the chest wall as herpes zoster, diseases of the breast, mastectomy and thoracotomy. These act through inhibition of PIH.

The commonest causes are pituitary adenoma (40-50%) and idiopathic hyperprolactinaemia.

GYNAECOLOGICAL DISORDERS ASSOCIATED WITH HYPERPROLACTINAEMIA

1. Amenorrhoea. Prolactin inhibits the pulsatile secretion of gonadotrophin releasing hormone, renders the ovary refractory to the action of pituitary gonadotrophins and inhibits ovarian steroidogenesis. About 20% of cases of secondary amenorrhoea are due to hyperprolactinaemia.
2. Oligomenorrhoea.
3. Dysfunctional uterine bleeding.
4. Anovulatory cycles. About 15% of cases of anovulation are due to hyperprolactinaemia.
5. Luteal phase defect (LPD) due to lysis of the corpus luteum (luteolysis).
6. Infertility due to anovulation and LPD.
7. Galactorrhoea. It is persistent secretion of milk or serous fluid from the breast in absence of breast-feeding. The serous fluid is clear, but may be yellow or green. It is bilateral and rarely unilateral. However, only 30-60% of women with high serum prolactin have galactorrhoea. Sometimes galactorrhoea occurs with a normal prolactin level indicating hypersensitivity of the breast tissue to the hormone. To detect galactorrhoea each quadrant of the breast should be squeezed from the periphery towards the nipple in an attempt to get a discharge. A discharge from the nipple may result from many causes, but true galactorrhoea is indicated by the presence of fat droplets demonstrated by microscopic examination or by the use of fat stains.
8. Premenstrual syndrome. Hyperprolactinaemia has been suggested as a cause.
9. Hirsutism. Prolactin increases the formation of adrenal androgens, and decreases the synthesis of sex-hormone binding globulin thus increasing free testosterone.
10. Loss of libido.
11. Severe hyperprolactinaemia (>100 ng/ml) usually leads to amenorrhoea and a hypoeostrogenic state. Oestrogen deficiency leads to osteoporosis in the long run.

DIAGNOSIS

1. History and physical examination. Exclude drugs which raise the serum prolactin.
2. Serum prolactin should be determined in the following conditions (a) amenorrhoea (primary and secondary); (b) oligomenorrhoea; (c) galactorrhoea; (d) infertility due to anovulation and luteal phase defect. A high level should be confirmed at least twice, as the level is raised by stress including attending hospital.
3. Primary hypothyroidism is excluded by measuring serum thyroid stimulating hormone (TSH) which is elevated.
4. Pituitary adenoma is excluded by computerized tomography (CT) scan of the sella turcica. Magnetic resonance imaging (MRI) is more accurate than CT scan but is costly. MRI detects all macroadenomas (more than 1 cm in diameter) and around 70% of microadenomas (less than 1 cm in diameter). A cone view of the sella turcica is done if CT scan and MRI are not available. In this case a macroadenoma will cause distortion,

expansion (ballooning) or erosion of the sella turcica. A cone view does not diagnose a microadenoma.

Notes

- Cone view means anteroposterior and lateral x-ray films of the sella turcica.
- Repeated CT scans may lead to cataract. Maximum 6 examinations in a life time are allowed.
- A prolactin level above 100 ng/ml occurs with a pituitary adenoma. However, a lower level less than 100 ng/ml may occur with a small microadenoma.
- Nanogram = milligram. mIU = milli international unit.

TREATMENT

1. Treatment of the cause as primary hypothyroidism and stop the use of any causative drug.
2. Idiopathic hyperprolactinaemia is treated by dopamine agonists which include:
 - a. Bromocriptine (Parlodel). It is an ergot alkaloid. The tablet is 2.5 mg. The recommended dose is 2-3 tablets (5-7.5 mg) daily, however, larger doses may be needed (up to 6 tablets). It has ergotamine-like side effects leading to nausea, vomiting, postural hypotension, dizziness and constipation. To avoid nausea and vomiting, it must be given with meals and we start with half tablet and gradually increase by half tablet every week. The drug can be given vaginally to avoid nausea and vomiting. The drug disappears from blood after 14 hours, and so it is given 2 or 3 times daily. Bromocriptine is also available in a long-acting injection form which is given intramuscularly in a dose of 50 or 75 mg every month. The injection gives a rapid response than the oral route.
 - b. Lisuride (Dopergin). It is more potent and causes less nausea and vomiting. The tablet is 0.2 mg.
 - c. Cabergoline (Dostinex). It causes less nausea and vomiting. It is long-acting and given once weekly, and if necessary twice weekly. The tablet is 0.5 mg. The dose is 0.5-3 mg (1-6 tablets). It can also be administered vaginally for the rare patient who cannot tolerate it orally.
 - d. Quinagolide (Norprolac). A nonergot preparation and so the side effects are few. The tablets are 25, 50, and 75 micrograms. The dose is 75-300 µg once daily. Untested in pregnancy.

Serum prolactin is repeated every 6 months, and CT scan or MRI every 1-2 years as a microadenoma may appear.

3. Pituitary adenoma. Both microadenoma and macroadenoma are treated medically by a dopamine agonist as bromocriptine, which leads to shrinkage of the tumour. Treatment is continued for life, because discontinuation leads to recurrence of symptoms. However, if a microadenoma is discovered accidentally and is not producing symptoms, no treatment is given, and the woman is kept under observation. She is seen once every year to exclude appearance of symptoms, and a cone view of the sella turcica is performed. Surgical treatment is indicated in case of macroadenoma if (a) the tumour does not decrease in size with medical treatment; (b) the patient cannot tolerate the side effects of medical

treatment; and (c) when vision is affected by the tumour compressing the optic chiasma. Radiotherapy is applied for cases recurring after surgery and when the patient is unfit for surgery when indicated.

Notes for the postgraduate

- Patients who conceive in the presence of a pituitary macroadenoma should continue bromocriptine and should have the visual fields examined every trimester as the tumour may enlarge under the effect of oestrogen (risk 1% with microadenoma and 15% with macroadenoma). The drug is not teratogenic.
- In the past when estimation of serum prolactin was not possible three syndromes were described. The Chiari-Frommel syndrome was applied to amenorrhoea-galactorrhoea following delivery. Ahmada-Del-Castillo syndrome was applied to amenorrhoea-galactorrhoea in the nullipara. Forbes-Albright syndrome indicating the same disorder in a patient with pituitary adenoma. These syndromes are of historic interest and are due to hyperprolactinaemia due to any cause which leads to amenorrhoea and galactorrhoea.
- No harm results from breast feeding, if the patient is having a pituitary adenoma.
- Hyperprolactinaemic women can use low-dose combined oral contraceptives for birth control. The low-oestrogen dose will not increase prolactin secretion, and will not increase the growth of a pituitary microadenoma.
- The success rate of treatment of anovulation due to hyperprolactinaemia is very high (about 90%), and the response is rapid.
- Bromocriptine stimulates dopamine D_2 -receptors leading to inhibition of prolactin secretion. The side effects are mainly due to stimulation of dopamine D_1 -receptors, serotonin, and α_1 -adrenergic receptors. Norprolac stimulates only D_2 -receptors and so side effects are few.
- Galactorrhoea is investigated in every woman. However, in a lactating woman, investigation is carried out one year after weaning.

ABNORMAL UTERINE BLEEDING

This includes polymenorrhoea, menorrhagia, metrorrhagia, menometrorrhagia and intermenstrual bleeding.

POLYMENORRHOEA

It is frequent menstruation. The menstrual cycle is less than 21 days.

Aetiology

Polymenorrhoea is due to a short proliferative or a short secretory phase. The short proliferative phase results from early maturation of the graafian follicle which may result from pituitary hyperstimulation. The short secretory phase is due to early degeneration of the corpus luteum, and is the result of:

1. Ovarian congestion as a part of pelvic congestion as in case of fibroids, retroversion, chronic pelvic infection, etc.
2. Hypothyroidism.



3. Dysfunctional polymenorrhoea occurring shortly after menarche, near the menopause, after abortion or labour. The early degeneration of the corpus luteum occurs in the absence of an organic cause.

Treatment

1. Progestogens given in the second half of the cycle, as norethisterone (Primolut-N tablets) 10 mg daily for 10 days starting on day 15 of the cycle.
2. A combined oral contraceptive is given for 21 days each month.
Hormonal treatment is given for 3 successive months to prevent recurrence of abnormal bleeding.
3. Thyroxine if there is hypothyroidism.
4. Treatment of anaemia if present.

MENORRHAGIA

It is excessive and/or prolonged menstruation. Menstruation is excessive if the amount of menstrual blood is greater than 80 ml. Menstruation is prolonged if bleeding continues for more than 7 days.

Aetiology

A. General Causes

(1) Hypertension; (2) congestive heart failure; (3) blood diseases as leukemia, thrombocytopenia, and von Willebrand disease; (4) hypo- and hyperthyroidism; (5) anticoagulant therapy; (6) liver disease particularly cirrhosis (may impair metabolism and excretion of oestrogen leading to hyperoestrinism, endometrial hyperplasia and menorrhagia. Also clotting factors may be affected with cirrhosis. There is also decreased synthesis of sex-hormone binding globulin leading to increased free oestrogen); (7) psychological disturbances (acting through the hypothalamus or through the autonomic nervous system affecting uterine blood vessels leading to pelvic congestion); (8) smoking leading to anovulation and unopposed oestrogen effect.

Note. Hypertension leads to menorrhagia when it is associated with atherosclerosis of the uterine vessels.

B. Local Causes

All causes of pelvic congestion:

(1) chronic pelvic infection as salpingitis; (2) pelvic tumours; (3) abnormal position of uterus as retroversion or prolapse; (4) simple pelvic congestion as in chronic constipation; (5) pelvic congestion syndrome due to broad ligament varicocele; (6) endometriosis and adenomyosis; (7) extragenital causes as chronic appendicitis.

Also menorrhagia is a common complication of intrauterine contraceptive devices and may complicate tubal sterilization. The abnormal uterine bleeding which may follow tubal

sterilization is explained by interference with ovarian blood supply leading to luteal phase defect or it is due to the effect of aging as the procedure is often done after the age of 35. Menorrhagia may also occur with a bicornuate uterus, due to increased surface area of the endometrium.

C. Dysfunctional Menorrhagia

Bleeding occurring in absence of an organic cause. It is due to irregular ripening or irregular shedding of the endometrium. In case of irregular ripening there is poor function of the corpus luteum so the endometrium is without enough hormonal support and bleeding starts several days before menstruation. Premenstrual endometrial biopsy will show mixed proliferative and secretory changes. In case of irregular shedding, there is slow and incomplete degeneration of the corpus luteum, so bleeding continues for several days after the proper flow. When the endometrium is examined on the 4th or 5th day of menstruation, it will show areas of secretory changes while the endometrium should be in the early proliferative phase. Sometimes we have anovulatory menorrhagia.

Treatment

1. General treatment. Rest in bed. Blood transfusion may be needed in severe cases. Correction of anaemia.
2. Treatment of the cause as hypertension.
3. Non-hormonal treatment:
 - a. Antifibrinolytic agents can be given because the fibrinolytic activity in the endometrium is increased in case of menorrhagia. They reduce the menstrual blood loss by 50% in most of the cases. Tranexamic acid (Cyklokapron tablets, 500 mg) is given as 1 g (2 tablets) orally 2-4 times daily during the period. Contraindicated if there is a previous history of thromboembolic disease.
 - b. Antiprostaglandins as ibuprofen (Brufen tablets, 400 mg three times daily during the period). The menstrual blood loss is reduced by about 25%. In case of menorrhagia, there is increased production of prostaglandin (PG) E_2 and prostacyclin (PGI_2). PGE_2 is a vasodilator and prostacyclin causes vasodilatation and prevents aggregation of platelets which is necessary for thrombus formation.
 - c. Haemostatic agents as diosmin (Daflon) and ethamsylate (Dicynone) tablets. The tablet is 500 mg. Two tablets are given twice daily during the bleeding. The drugs act by decreasing capillary fragility and increasing aggregation of platelets.
4. Hormonal treatment:
 - a. Progestogens as norethisterone (Primolut-N) tablets. The tablet is 5 mg. The dose is 10-15 mg (2-3 tablets) daily for 20 days. When treatment is stopped shedding of the endometrium and withdrawal bleeding occurs, i.e., medical curettage. Progestogens are of value in cases of anovulatory bleeding (absent progesterone) and luteal phase defect (inadequate production of progesterone). Medroxyprogesterone acetate

- (Provera) tablets can also be used (it is non-androgenic). To prevent recurrence of bleeding we give 10 mg daily for 10 days in the second half of the cycle every month for at least 3 successive months.
- b. Combined oral contraceptives. One tablet is given 2 or 4 times daily until the bleeding stops, then one tablet daily for 20 days. They act by creating atrophic endometrium. The tablets are then given in the usual way for at least 3 successive months.
 - c. Danazol. It is a weak synthetic androgen. The dose is 200 to 400 mg daily and continuously for 3 months. The 200 mg daily reduce the menstrual blood loss by 50%, while the 400 mg daily usually lead to amenorrhoea. The drug is very expensive and has many side effects, however, it can be used when the combined oral contraceptives and progestogens are contraindicated, or ineffective (intractable menorrhagia).
 - d. Gestrinone. It is a weak synthetic androgen which acts like danazol and has the same side effects. The dose is 1.25-2.5 mg given twice weekly for 3 months.
 - e. Thyroxine is given if there is hypothyroidism.
 - f. Gonadotrophin releasing hormone analogues (agonists). They lead to amenorrhoea. They are given as daily nasal spray, or intramuscular or subcutaneous injections every 4 weeks for 3 successive months. They can be used for intractable menorrhagia..
 - g. Induction of ovulation with clomiphene citrate (Clomid). This may help in case of anovulatory bleeding. However, it is used only if the patient desires pregnancy.
 - h. Progesterone or levonorgestrel releasing intrauterine device (Mirena IUD). It can be applied to reduce blood loss particularly in cases of chronic renal failure, blood dyscrasias, kidney and liver transplant to avoid the metabolic and systemic side effects of sex hormones. Mirena device reduces menstrual blood loss by more than 80%.
5. Surgical treatment:
- a. Uterine curettage. Indications: (a) If the bleeding is severe; (b) if it fails to respond to other lines of treatment; (c) if the patient is above 40 to exclude endometrial carcinoma. The advantages are (a) it arrests bleeding in about 60% of cases by removing the necrotic endometrium, (b) it determines the type of dysfunctional bleeding, (c) may reveal an organic cause as endometrial carcinoma.
 - b. Hysterectomy. Indicated when all lines of treatment fail including repeated curettage at least twice.
 - c. Endometrial ablation. It is performed when hysterectomy is refused and when the patient is unfit for hysterectomy as in case of marked obesity, severe hypertension, or diabetes mellitus. The endometrium is destroyed by laser, thermal ablation, as well as other methods.

METRORRHAGIA

It is irregular uterine bleeding not related to menstruation. The causes are: (1) local lesion in the genital tract which may be traumatic, inflammatory or neoplastic; (2) complications of pregnancy as abortion and hydatidiform mole; (3) irregular intake of hormones or

contraceptive tablets; (4) the presence of intrauterine device; (5) dysfunctional metrorrhagia as in metropathia haemorrhagica and threshold bleeding.

MENOMETRORRHAGIA

It is menorrhagia associated with irregular intermenstrual bleeding.

INTERMENSTRUAL BLEEDING

It is bleeding that occurs between normal menstrual cycles.

Note for the postgraduate

Thyroid disorders lead to abnormal uterine bleeding by several mechanisms: (1) hyperthyroidism leads to rapid excretion of oestrogens in urine; (2) thyroxine may have a direct effect on the spiral arterioles of the endometrium, and on haemostasis during menstruation; (3) hyperthyroidism increases the liver synthesis of sex-hormone binding globulin (SHBG) and thus decreases free serum oestradiol (hypoestrogenic state). Hyperthyroidism commonly leads to amenorrhoea and oligomenorrhoea, but can also lead to menorrhagia. Hypothyroidism decreases the SHBG and increases free serum oestradiol. Hypothyroidism commonly leads to menorrhagia, but can also lead to amenorrhoea and oligomenorrhoea. Primary hypothyroidism may cause hyperprolactinaemia which can lead to amenorrhoea.

METROPATHIA HAEMORRHAGICA (SCHROEDER DISEASE)

Aetiology

The exact cause is unknown. The graafian follicle fails to rupture, and continues to grow to form a cyst. Large amounts of oestrogen are produced which act on the uterus. When oestrogen reaches a high level it inhibits the secretion of FSH of the anterior pituitary and this is followed by degeneration of the cystic follicle and drop in the level of oestrogen resulting in separation of the endometrium and withdrawal bleeding, or the endometrium grows so thick that its blood supply becomes inadequate leading to necrosis and sloughing.

Pathology

1. The Uterus

It is slightly symmetrically enlarged and soft in consistency due to increased vascularity. There is hypertrophy of the myometrium. The endometrium is thickened, haemorrhagic and may become polypoidal. Microscopically, the endometrium shows simple hyperplasia (cystic glandular hyperplasia): (a) the glands are increased in number and become cystic and lined by cuboidal or columnar epithelium; (b) there is variation in the size of the glands giving a "Swiss cheese" appearance; (c) no evidence of secretory changes; (d) the stroma is dense and oedematous; (e) areas of necrosis and haemorrhage may be seen.

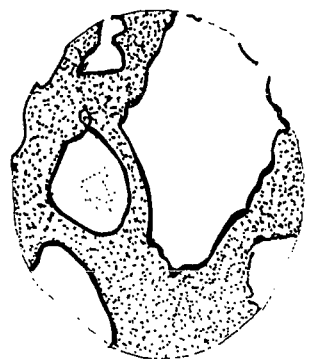


Fig.26. Cystic hyperplasia of the endometrium

2. The Ovaries

One ovary is enlarged and cystic. It contains one or multiple follicular cysts lined by granulosa cells. A corpus luteum is absent. The cysts may be bilateral. The cysts are less than 5 cm in diameter, i.e., functional cysts.

Note. Cystic glandular hyperplasia is an old term and has been replaced by simple endometrial hyperplasia.

Diagnosis

Age Incidence

The condition is more common near the menopause or shortly after menarche.

Symptoms

There is severe painless uterine bleeding unrelated to menstruation. It may continue for several days or weeks. In about 50% of cases the bleeding is preceded by a short period of amenorrhoea lasting 6-8 weeks. In other cases it is preceded by menorrhagia or normal menstruation. Symptoms of anaemia may be present. Bleeding is painless because it is anovulatory.

Signs

The uterus is slightly symmetrically enlarged and soft. One or both ovaries may be felt enlarged and cystic.

Investigations

1. Ultrasonography shows enlarged uterus, thick myometrium, thick endometrium, and follicular cysts in one or both ovaries. The cysts are less than 5 cm in diameter.
2. Endometrial biopsy confirms the diagnosis by showing the picture of simple endometrial hyperplasia.

Differential Diagnosis

Causes of uterine bleeding associated with symmetrically enlarged uterus as abortion, ectopic pregnancy and submucous fibroid.

Treatment

The same lines of treatment mentioned with menorrhagia.

THRESHOLD BLEEDING

In this case the endometrium is thin with a poorly developed proliferative phase. The ovary is producing small amounts of oestrogen which reach the threshold for bleeding but not enough to produce a full proliferative phase. The suggested oestrogen level which causes bleeding is a serum level between 50 and 100 picograms/ml. A level below 50 or above 100 pg/ml is associated with amenorrhoea. The clinical picture is like metropathia haemorrhagia

and differentiated only by uterine sonography and curettage. Treated by oestrogen given for 21 days with a progestogen added during the last week of therapy. Treatment is repeated for 3 months.

Note. Metropathia haemorrhagia = irregular uterine bleeding + too much oestrogen and no progesterone. Threshold bleeding = irregular uterine bleeding + too little oestrogen and no progesterone.

DYSFUNCTIONAL UTERINE BLEEDING (DUB)

Definition

It is abnormal uterine bleeding occurring in the absence of any systemic or organic cause in the genital tract. The dysfunction may arise in the endometrium, ovary, pituitary, hypothalamus or higher centres.

Notes

- The endometrial dysfunction is related to excessive production of prostaglandin E_2 and prostacyclin or increased fibrinolytic activity of the endometrium. PGE_2 causes vasodilatation and relaxation of the nonpregnant uterus (but contraction of the pregnant uterus). Prostacyclin (PGI_2) causes vasodilatation and inhibits platelet aggregation.
- Systemic causes as thyroid dysfunction and bleeding disorders.

Age incidence

It is more common near the menopause (50% of the cases), or shortly after menarche (20% of the cases). More common near menopause due to decreased number of ovarian follicles and their increased resistance to gonadotrophin stimulation. More common shortly after menarche due to immaturity of the hypothalamic-pituitary-ovarian axis.

Classification

Clinically, the bleeding may be cyclic in the form of menorrhagia or polymenorrhoea, or it may be acyclic as in case of metropathia haemorrhagica and threshold bleeding. According to the histological picture of the endometrium, the bleeding may be ovulatory when the endometrium shows secretory changes or anovulatory in absence of the latter. Metropathia haemorrhagica and threshold bleeding are examples of anovulatory bleeding.

Endometrial Histology in DUB

The endometrium may be proliferative, hyperplastic, atrophic, secretory or mixed which is partly proliferative and partly secretory.

Diagnosis

A. History

Personal history

1. Age of the patient, dysfunctional bleeding is more common near the menopause or shortly after menarche.
2. Marital state to exclude complications of pregnancy as abortion.

Present history

Ask about the amount, character, and duration of bleeding, its type whether cyclic or acyclic. The presence of other symptoms as pain and foul discharge, urinary and gastrointestinal symptoms.

Past history

1. Diseases as hypertension, heart failure, haemorrhagic blood diseases as leukemia, and inherited bleeding disorders as von Willebrand disease.
2. Contraceptive tablets intake.

Menstrual history

If bleeding is preceded by a short period of amenorrhoea suspect pregnancy or metropathia haemorrhagica.

Obstetric history

A recent abortion, labour, or passage of a hydatidiform mole may direct attention to choriocarcinoma.

B. General Examination

For signs of anaemia, signs of bleeding disorders in the form of bruising and petechiae, presence of cachexia, and the presence of a general cause as hypertension or thyroid disease.

C. Abdominal Examination

For a pelvi-abdominal mass as fibroid or pregnancy.

D. Pelvic Examination

To detect a local cause for the bleeding. The urethra and anal canal are excluded as a source of bleeding as urethral caruncle or piles. If no general or local cause is found to explain bleeding, it is provisionally diagnosed as dysfunctional. However, further investigations may show an organic cause.

E. Special Investigations

1. Transvaginal sonography. It excludes the presence of an ovarian tumour or a lesion in the uterus as fibroids or endometrial carcinoma.
2. Cervical smear. Taken in absence of bleeding to detect the presence of malignant cells which may come from the cervix, endometrium, tubes, or ovaries.
3. Endometrial biopsy. This must be done in every woman above the age of 40 years complaining of abnormal uterine bleeding, as it is the only sure method to exclude endometrial carcinoma. Endometrial biopsy is taken by one of three methods; fractional uterine curettage, endometrial aspiration (using Pipelle suction curette or Vabra aspirator), or hysteroscopy.

4. Laboratory tests. These are done according to the clinical findings and include:
 - a. Complete blood count.
 - b. Platelet count, bleeding time, coagulation time, estimation of clotting factors if a bleeding disorder is suspected from the history or clinical examination.
 - c. Thyroid function tests if we suspect a thyroid disorder.
 - d. Liver function tests if we suspect a liver disease.
 - e. Serum progesterone done on day 22-24 to diagnose luteal phase defect and anovulation.
5. Laparoscopy. It is indicated when treatment fails to control bleeding. It may reveal an organic cause in the pelvis as a small oestrogenic ovarian tumour.

Treatment

- Treatment of polymenorrhoea: See page 72.
- Treatment of menorrhagia and metrorrhagia: See page 73.
- Treatment of threshold bleeding. See page 76.

POSTMENOPAUSAL BLEEDING

It is bleeding from the genital tract occurring 6 months or 1 year by some gynaecologists or more after menopause. It is a serious symptom because in about 25% of cases, it is due to a malignant lesion in the genital tract.

Prevalence

About 7 per 1000 postmenopausal women.

Aetiology

(A) General Causes

(1) Oestrogen therapy (25%). Oestrogen given for menopausal symptoms may lead to withdrawal bleeding; (2) blood diseases as leukemia; (3) anticoagulant therapy; (4) Ginseng is obtained from the root of some plants, and is included in some tonics and antioxidants. It has a weak oestrogenic effect and may cause bleeding.

(B) Local Causes

1. **Vulva.** Malignant tumour, fissured leucoplakia, urethral caruncle, and direct trauma.
2. **Vagina.** Malignant tumour, senile vaginitis, trophic ulcer in prolapse, and retained foreign body or pessary in the vagina.
3. **Cervix.** Malignant tumour, erosion and ulcers.
4. **Uterus.** Malignant tumour, senile endometritis, tuberculous endometritis, fibroid undergoing malignant change or a fibroid polyp showing necrosis at its tip or endometrial hyperplasia resulting from unopposed oestrogen action, the source of which is an oestrogenic ovarian or adrenal tumour or peripheral conversion of

androgens to oestrogens mainly occurring in body fat as in case of obese women who are liable to develop endometrial carcinoma.

5. **Tube.** Carcinoma. This leads to a watery vaginal discharge which finally becomes blood stained.

6. **Ovary.** Carcinoma with metastases in the endometrium and oestrogenic ovarian tumours.

(C) In about 15% of cases no cause is found after physical examination and uterine curettage which shows atrophic endometrium.

Diagnosis

A. History

Personal history

(a) Age: The commonest age incidence for carcinoma of uterus is 55-70 years while that for carcinoma of the vulva is 60-70 years; (b) parity: some tumours are more common among nulliparae e.g. endometrial and ovarian carcinoma.

Present history

Ask about the amount, character and duration of bleeding, duration of menopause, and the presence of other symptoms as pain and foul discharge, urinary and gastrointestinal symptoms (malignant invasion of bladder or bowel).

Past history

(a) Oestrogen therapy; (b) diseases as diabetes mellitus, hypertension and blood diseases as leukemia. Endometrial carcinoma is more common in diabetic hypertensive patients.

Family history

Carcinoma of the body of the uterus and ovary have a familial tendency.

B. General Examination

(1) Signs of anaemia; (2) signs of bleeding disorders; (3) presence of cachexia; (4) examination of heart and chest for secondaries; (5) estimation of blood pressure.

C. Abdominal Examination

For a pelvi-abdominal mass and ascites which is common with ovarian malignancy.

D. Pelvic Examination

To detect a local cause for bleeding. The urethra and anal canal are excluded as being the source of bleeding as urethral caruncle or piles.

E. Special Investigations

1. Transvaginal sonography. It excludes the presence of an ovarian tumour or a lesion in the uterus as endometrial carcinoma.

2. Cervical smear. Taken in absence of bleeding to detect the presence of malignant cells which may come from the cervix, endometrium, tubes, or ovaries.
3. Endometrial biopsy. It must be done in every case of postmenopausal bleeding, as it is the only sure method to exclude endometrial carcinoma. Endometrial biopsy is taken by one of three methods; fractional uterine curettage, endometrial aspiration, or hysteroscopy:
 - a. Fractional uterine curettage. Separate specimens are taken from the cervical canal and body of uterus. It excludes endocervical carcinoma and endometrial carcinoma which may be extending to the cervix.
 - b. Endometrial aspiration. The Vabra aspirator or Pipelle suction curette is used to obtain endometrial tissue by suction by creating a negative pressure. The advantages over uterine curettage are: (1) done without anaesthesia which may be contraindicated by the presence of marked obesity, hypertension, or diabetes mellitus, so it is done as an outpatient procedure; (2) less cost; (3) complications as perforation are less. Endometrial aspiration detects endometrial carcinoma in about 95% of cases, and has replaced uterine curettage for the diagnosis of postmenopausal bleeding.
 - c. The use of hysteroscope. The hysteroscope inspects the uterine cavity and endocervix and can show small tumours missed by uterine curettage. Hysteroscopy is followed by full uterine curettage or directed endometrial biopsy from abnormal areas. It can be done without anaesthesia as an outpatient procedure (office hysteroscopy) using a flexible hysteroscope.
4. Biopsy is taken from any suspected lesion in the vulva, vagina, or cervix.
5. Laboratory tests. These are done according to the clinical findings and include:
 - a. Complete blood count.
 - b. Platelet count, bleeding time, coagulation time, estimation of clotting factors if a bleeding disorder is suspected.

Notes for the postgraduate

- Endometrial carcinoma is responsible for about 10% of postmenopausal bleeding.
- Only about 50% of endometrium is obtained after full uterine curettage, and so small tumours may be missed.
- In some postmenopausal patients, it may be difficult to enter the uterine cavity, due to cervical stenosis, acute ante flexion or retroflexion of the uterus. In this case, the bladder is filled with 300 ml of sterile physiologic saline. The uterine sound, dilators, and curette can now be introduced safely inside the uterine cavity under transabdominal ultrasound control. The full bladder helps to reduce the acute ante flexion.

Treatment

It is treatment of the cause. If no cause can be detected the patient should be followed up. If bleeding recurs it is better to do hysterectomy and bilateral salpingo-oophorectomy which may reveal a missed early carcinoma of uterus or tube.

UTERINE BLEEDING ACCORDING TO AGE

1. In the newborn. Oestrogens obtained from the mother may cause withdrawal bleeding in the first week of life (birth crisis). It disappears within few days.
2. During childhood, bleeding may be due to precocious puberty from any cause, foreign body in the vagina or the rare "grape-like" sarcoma of the cervix or vagina.
3. Bleeding in adolescent girls (under the age of 20) is dysfunctional in most cases. However, bleeding disorders as von Willebrand disease, and complications of pregnancy must be ruled out.
4. In the childbearing period (20-40 years), complications of pregnancy as abortion, and ectopic pregnancy are the commonest causes of bleeding. Dysfunctional uterine bleeding, and use of contraceptives are other causes.
5. Perimenopausal bleeding (women over 40 years) is commonly dysfunctional bleeding or due to an organic cause as fibroids or carcinoma of the cervix.
6. Postmenopausal bleeding is due to malignant tumour in the genital tract in about 25% of cases. Also bleeding may result from hormone replacement therapy. However, senile vaginitis is the commonest cause of postmenopausal bleeding.

Note. The perimenopause is the period immediately prior to menopause and the first 6 months or 1 year (by some gynaecologists) after menopause.

SECTION IV

TRAUMATIC LESIONS

OLD COMPLETE PERINEAL TEAR

SYMPTOMS

There is loss of voluntary control over the passage of faeces and flatus. However, many women try to use the levator ani muscles as a sphincter and can control the passage of hard stools but remain incontinent to flatus and liquid stools. Vaginitis and vaginal discharge are usually present due to irritation by faecal matter.

SIGNS

1. A tear is seen in the perineum which extends from the vagina to the anal opening.
2. There is a dimple on each side of the anus indicating the retracted torn ends of the external anal sphincter.
3. The normal radial folds around the anus are absent except posteriorly.
4. The index finger can be introduced easily without resistance into the anus indicating absence of the sphincteric control.

TREATMENT

Operation is done to repair the tear.

a. Preoperative Preparation

Any infection in the cervix or vagina must be treated before operation. The repair is done 3-6 months after labour to allow healing of infected granulation tissue, absorption of scar tissue, and the tissues become strong enough to hold the sutures. The patient is admitted to hospital 3 days before operation during which the following treatment is given:

1. A fluid diet. Milk is not given to avoid distension.
2. An intestinal antiseptic as neomycin (1 gm every 6 hours), and metronidazole (250 mg tid) must be given to act on aerobic and anaerobic bacteria.
3. A daily vaginal douche and a saline enema twice daily.

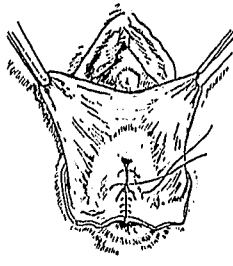
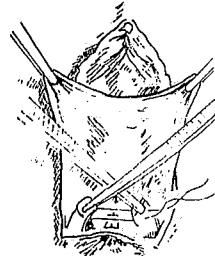
b. Operation

An H-shaped incision is made in the skin with the transverse limb at the ano-vaginal junction. The incision is deepened to expose the various structures of the perineal body. The vagina is separated from the rectum and the ends of the external anal sphincter are identified. The wall of the rectum and anal canal is closed from above downwards by thin chromic catgut (2/0) using interrupted Lambert sutures avoiding the mucosa. The torn ends of the external anal sphincter are brought together anterior to the anus by two stitches of thick chromic

catgut. The levator ani muscles are approximated by interrupted chromic catgut sutures. The vagina is closed by interrupted chromic catgut sutures. The superficial perineal muscles are approximated by chromic catgut. The perineal skin is closed by interrupted or subcuticular chromic catgut. Delayed-absorbable sutures as Vicryl or Dexon can be used instead of chromic catgut to close the different layers of the tear. These sutures cause less tissue reaction and infection compared with the catgut.



Dimple

H-shaped
incisionClosure of
rectumEnds of external
anal sphincterFig.27. Old complete
perineal tearFig.28. Repair of old complete
perineal tear

c. Postoperative Care

1. The perineal wound is kept clean and dry. After each micturition or defecation, the perineum is washed with antiseptic solution as Savlon, and covered by sterile vulval pad.
2. Nothing by mouth for 48 hours, only intravenous fluids are given. Then oral fluids are given for 3 days. Milk is not given to avoid distension.
3. An antibiotic, e.g., cephalosporin is given to guard against wound infection.
4. On the fifth night give a castor oil purge (60 ml). Then the patient is given liquid paraffin for 2 weeks to avoid constipation.
5. No sexual intercourse for 3 months.
6. In subsequent delivery a mediolateral episiotomy is done if indicated (but not elective episiotomy).

GENITOURINARY FISTULAE

Abnormal communications between the urinary and genital tracts are classified according to their anatomical situations into the following types:

- A. Ureteric:
 1. Ureterouterine.
 2. Ureterocervical.
 3. Ureterovaginal.

B. Vesical:

1. Vesicouterine.
2. Vesicocervical.
3. Vesicovaginal.

C. Urethral:

Urethrovaginal.

The commonest type is the vesicovaginal then the ureterovaginal fistula. More than two organs may be involved, e.g. vesicourethrovaginal fistula. Urethrovaginal fistula results from vaginal operations in which the urethra is damaged.

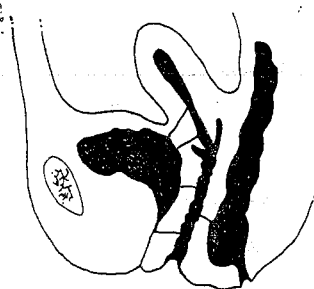


Fig.29. Genitourinary fistulae

VESICOVAGINAL FISTULA

Incidence

The incidence of fistulae varies from country to country, the same applies to the aetiological factors. Accurate figures may be difficult to obtain in some parts of the world. However, about 350 vesicovaginal fistulae are treated each year in England and Wales.

Aetiology

A. Congenital. This is very rare.

B. Traumatic. Due to different types of trauma:

1. Obstetric Trauma

This is the commonest cause of vesicovaginal fistula in Egypt and other developing countries. Obstetric trauma leads to two types of fistula:

- i. Necrotic obstetric fistula. Due to obstructed labour which leads to prolonged compression, ischaemia and necrosis of the soft tissues between the fetal head and pelvic walls. The necrotic tissue takes some days to separate, so incontinence of urine occurs about 3-10 days after delivery. Also a necrotic fistula may occur when the bladder is included during suturing the lower uterine segment in caesarean section.
- ii. Traumatic obstetric fistula. The bladder may be directly injured during caesarean section. Forceps delivery may lead to a vaginal or cervical tear which may extend to involve the urethra, the bladder or ureter. Also the bladder may be injured by the perforator or spicules of bones after craniotomy. In traumatic fistula, incontinence of urine occurs immediately after delivery.

2. Surgical Trauma

Fistula may occur after total abdominal hysterectomy, vaginal hysterectomy, Wertheim operation, anterior colporrhaphy and McIndoe operation to create an artificial vagina. Surgical trauma, especially hysterectomy, is the most common cause of vesicovaginal fistula in developed countries.

3. Direct Trauma

As falling on sharp objects, fracture of the pelvis and defloration injuries. Neglected foreign body or vaginal pessary may lead to ulceration and fistula formation.

C. Inflammatory

As in case of syphilis, bilharziasis or tuberculosis of the bladder or vagina. Lymphogranuloma venereum may be complicated by urinary or faecal fistula.

D. Neoplastic

Malignant tumour of the cervix, vagina or bladder. The commonest cause of a malignant vesicovaginal fistula is advanced cervical carcinoma.

E. Postirradiation

Radium applied for the treatment of carcinoma of the cervix or vagina may cause ischaemic necrosis and fistula. The fistula usually appears 3-9 months after irradiation and is surrounded by excessive scar tissue. However, the fistula can develop at a variable period after radiotherapy occasionally occurring up to 25 years after treatment.

Diagnosis

I. History

History can give idea about the aetiology of the fistula whether it is due to labour, surgery, irradiation, etc. Also, the history can differentiate between the different types of urinary incontinence which may be true, false (chronic retention with overflow), urgency or stress incontinence.

II. Symptoms

1. Incontinence of urine. It may be total or partial i.e. the patient can retain some urine in her bladder and passes it voluntarily. This occurs when the fistula is small or situated high in the bladder. This case has to be differentiated from a ureterovaginal fistula.
2. Soreness of the vulva and pruritus. The continuous dribbling of urine leads to vaginitis and vulvitis.
3. Pain may be felt in the suprapubic region and loin due to ascending infection causing cystitis and pyelonephritis.
4. Psychological disturbances as amenorrhoea because incontinence of urine is very distressing (amenorrhoea in association with fistula can be due to psychological disturbances, pregnancy or as a manifestation of Sheehan syndrome following difficult labour with postpartum haemorrhage).

III. Signs

1. General Examination

Patient is examined for evidence of renal failure. Signs of anaemia and malnutrition should be noted as these have to be corrected before surgical repair.

2. Abdominal Examination

The kidneys are palpated for tenderness or enlargement. Ascending infection may lead to pyelonephritis.

3. Vaginal Examination

a. Inspection

The continuous discharge of urine causes vaginitis and vulvitis. The skin of the vulva is wet and red and may become exfoliated and ulcerated. Phosphatic crystals may deposit on the skin of the vulva giving it a gritty sensation. Infection of the hair follicles (folliculitis) may ensue. The vaginal walls are red and wet.

b. Digital Palpation

The anterior vaginal wall is palpated with the patient in the dorsal position. A large fistula is easily felt by vaginal examination and a finger can be passed through the opening into the bladder. A small fistula cannot be felt but it is known by the presence of the surrounding fibrosis. We must determine the site of the fistula (high, mid or low), its size, the presence of more than one opening, the extent of scarring, the mobility of the fistulous tract and the capacity of the vagina.

c. Speculum Examination

The patient is examined by Sims speculum in Sims or left lateral position. This allows inspection of the anterior vaginal wall. A metal catheter or a sound may be passed along the urethra to see its tip from the vagina. In the past, they used to elicit "the Click test." A probe or sound is passed into the fistula from the vagina and made to touch a metal catheter in the bladder to give a clicking sound. In some cases the bladder mucosa becomes prolapsed and overhangs the edges of the fistula. If the fistula is small we fill the bladder with methylene blue solution and then inspect the anterior vaginal wall.

Note. In Sims position the patient lies on her left side with the left thigh and knee extended and her right thigh and knee flexed and left arm behind her back. Left lateral position is the same but the left arm is in front of the chest.

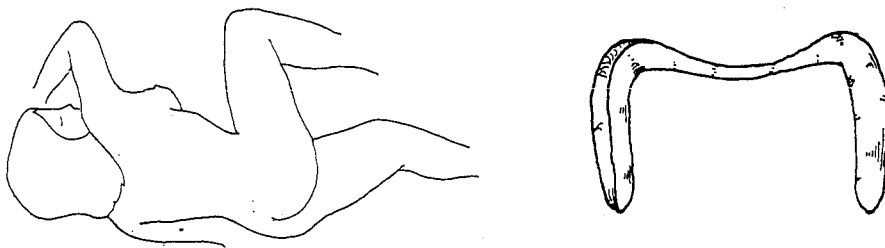
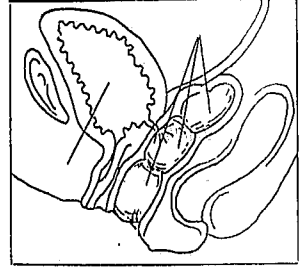


Fig.30 Sims position and Sims speculum

IV. Special Investigations

1. Methylene blue test

To differentiate between a small vesicovaginal fistula and ureterovaginal fistula or stress incontinence. Three pieces of gauze are inserted into the vagina. The bladder is filled with 200 ml of 1% sterile methylene solution using a rubber catheter which is then removed.



The patient is asked to walk around for a few minutes then the inner 2 pieces of gauze are examined. If they are stained blue, this means a vesicovaginal fistula, if soaked with urine, it is a ureterovaginal fistula. If the anterior vaginal wall is further inspected by Sims speculum, the coloured solution will outline the small vesicovaginal fistula. The lowest piece of gauze is discarded as it is usually stained during filling the bladder.

2. Intravenous Pyelography

It is done in very case to assess kidney function and to exclude a ureteric fistula.

3. Cystoscopy

It is done in every case. It diagnoses a small vesicovaginal fistula, shows the relation of the fistula to the ureteric openings in the bladder, excludes multiple fistulae and diagnoses a ureterovaginal fistula. To allow filling the bladder with sterile water, we put a finger or a pack in the vagina or the cystoscope is introduced with the patient lying in the knee chest position. This creates a negative intrabdominal pressure and allows distension of the bladder (indirect air cystoscopy). Also the male condom can be fixed to the tip of the cystoscope and is distended with sterile water after the cystoscope is introduced into the bladder.

Treatment

1. In case of inflammatory or malignant fistula, the treatment is that of the primary cause.
2. In congenital and traumatic fistula the treatment is operative closure. However, if the bladder is injured during labour, it is useless to close the fistula immediately because of oedema and friability of the tissues. However, we fix a Foley catheter in the bladder for three weeks and give antibiotics. The fistula may heal completely or is left smaller in size. Operation is then performed after 3-6 months to allow for healing of infected granulation tissue, absorption of scar tissue, and the tissues become strong enough to hold the sutures. Tissues damaged by radiation need longer time before surgical closure is attempted and we may wait up to one year due to the presence of excessive fibrosis. The best time for operation will be that time when the surgeon determines by palpation that the tissues are soft, pliable and can be mobilized. The use of cortisone preoperatively to shorten the waiting period by helping absorption of scar tissue is a matter of controversy.

A. Vaginal Operations

1. The Flap Splitting or Dedoublement Operation

The vagina is separated from the bladder and each organ is closed separately.

2. The Saucerization or Sims Operation

An elliptical incision is made in the vaginal wall. The edge of the fistula is excised obliquely removing a wider part of the vaginal than of the muscle wall of the bladder (no bladder mucosa is removed). The edges of both organs are simultaneously sutured using a single layer of non-absorbable material as nylon or silver wire. It is done for high inaccessible fistula surrounded by dense scar tissue as vault fistula after hysterectomy. In this case it is difficult to separate the vagina from the bladder.

3. Latzko Operation

It has the same indication as saucerization operation. A circular incision is made in the vaginal wall around the fistulous opening. The tract of the fistula is excised down to the bladder wall. Four incisions are now made in the vaginal wall and the 4 flaps made are excised. This allows mobilization of the bladder which is closed. This is followed by closure of the vagina. In this way the vaginal vault is obliterated (partial colpocleisis).

4. Postirradiation Fistula

The blood supply of the area is poor, so we transplant some tissue with intact blood supply between the bladder and vagina. We can use the gracilis muscle, the bulbocavernosus muscle (Martius graft) or a flap from the rectus abdominis.

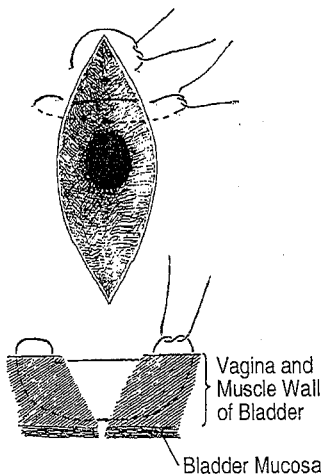


Fig. 31-2. Saucerization operation.

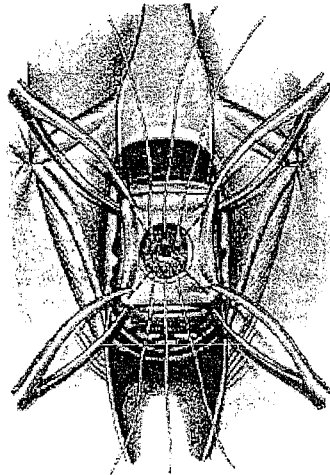


Fig. 31-3. Latzko operation.

B. Abdominal Operations

Indicated when vaginal operations fail or when the fistula is surrounded by excessive fibrosis, so separation of the bladder becomes difficult, also high fistulas which cannot be reached easily from below. The abdominal approach may be:

1. Extraperitoneal transvesical or
2. Intraperitoneal transvesical or
3. Intraperitoneal extravesical.

The transperitoneal approach is used where the extraperitoneal approach is difficult or an omental graft is indicated. Pfannenstiel or midline incision. However, if an omental graft will be needed we have to use a midline incision that can be extended enough to allow mobilization of the omental pedicle.

Preoperative Preparation

1. Complete blood count with correction of anaemia and all factors related to general health as diabetes and malnutrition.
2. Oestrogen locally or by mouth for atrophic tissues in postmenopausal patients.
3. Treatment of infection in the genital tract. Vulvitis which is often present acts as a septic focus and should be treated before operation. For this reason, the skin of the vulva and inner sides of the thighs is constantly covered with a thick layer of zinc oxide ointment or vaseline to prevent maceration of the skin by urine. Phosphatic deposits on the vulva are scraped and resulting ulcers are painted with silver nitrate or mercurochrome until healed. Cervicitis is treated by cautery.
4. Treatment of any urinary tract infection. Urine analysis, culture and sensitivity tests are performed. Urine is collected by a catheter if possible or we put a sterile piece of cotton in the vagina which is then removed and squeezed.
5. Kidney function tests. Blood urea, serum creatinine and intravenous pyelography should be performed.
6. Cystoscopy. Already mentioned.

Technique of Dedoublement Operation

1. General anaesthesia. However, spinal anaesthesia may be resorted to.
2. Posture. The patient is put in the elevated lithotomy position. The knee-chest position can be used if the fistula is adherent to the back of the symphysis pubis.
3. If the vagina is narrow a midline or mediolateral episiotomy (Schuchardt incision) is done and closed at the end of operation.
4. A circular incision is made in the vaginal wall around the fistula and 0.5 cm from its margin. From this incision, two longitudinal cuts are passed upwards and downwards in the vaginal wall. Before starting any incision, some prefer to inject a diluted solution of epinephrine in saline (1 in 200,000) to open up tissue planes and to act as a vasoconstrictor.

5. The vaginal wall is then separated from the bladder over a wide area, at least 1.5 cm all around the fistula. Separation is carried out by sharp dissection using the knife or a small curved sharp pointed scissors.
6. The opening in the bladder is closed using 2/0 chromic catgut or 3/0 delayed-absorbable sutures as Dexon or Vicryl. These sutures cause less tissue reaction and infection compared with the catgut. We use interrupted inverting Lembert sutures passing through the muscle wall of the bladder and avoiding the mucosa. This leads to inversion of the mucosa to allow healing. A second layer of interrupted sutures may be used. Some surgeons excise the fibrous tissue to freshen the edges of the fistula to leave a raw edge for better healing. A small rounded fistula may be closed by a purse-string suture.
7. Sterile methylene solution (100-200 ml) is injected into the bladder to be sure that it is water tight. If any leakage occurs, further sutures are taken.
8. The vagina is then closed by interrupted 2/0 chromic catgut or 3/0 delayed-absorbable sutures or by a nonabsorbable material as silk or nylon.
9. A Foley catheter is fixed to avoid distension of the bladder. However, some prefer suprapubic drainage or even combined drainage.
10. A vaginal pack may be inserted at the end of operation to help haemostasis and to avoid reactionary haemorrhage.

Note for the postgraduate

Suprapubic drainage using a Penrose catheter avoids trauma which may be caused by a urethral catheter. It also avoids catheterization which may be needed when the patient starts to pass urine.

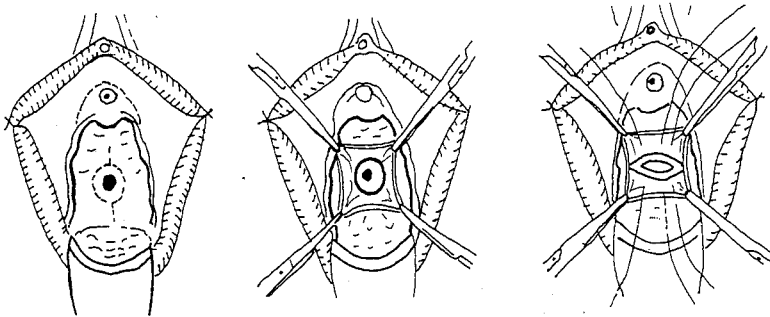


Fig. 32. Flap splitting operation

Postoperative Care

1. The catheter should be left for at least 10-14 days.
2. Observation of urine. Every 2 hours day and night, the nurse should record on a special chart the amount of urine, its colour and any precipitate. If there is no urine, this indicates either anuria or obstruction of the catheter. In the latter, there is suprapubic pain and the bladder is distended and felt as a cystic swelling in the lower abdomen. The catheter may be blocked by a plug of mucus, blood clot or deposits of phosphate if urine is alkaline. In

this case, the catheter is changed. A catheter specimen should be sent frequently to exclude urinary infection.

3. Antibiotics to prevent infection of urine and wound.
4. Large quantities of fluids, at least 3 litres daily.
5. If a vaginal pack was inserted, it is removed after 24 hours.
6. If nonabsorbable material was used to close the vagina, it is removed 21 days after operation and in the operating room and preferably under general anaesthesia.

Subsequent Management

1. After removal of the catheter, the patient must pass urine every 3 hours day and night to avoid distension of the bladder.
2. She must remain under observation in hospital for one month.
3. No sexual intercourse for 3 months. In fact nothing should enter the vagina for 3 months.
4. No pregnancy for at least one year, and during labour an upper segment caesarean section is performed to avoid recurrence of the fistula.

Causes of Failure of Operation

A. Causes before Operation

1. Presence of infection in the genital tract, vulvitis, vaginitis or cervicitis.
2. Presence of infection in the urinary tract.
3. Bad general condition due to anaemia, uncontrolled diabetes mellitus, etc.

B. Causes during Operation

1. Incomplete closure.
2. Excessive trauma to the tissues.
3. Eversion of the bladder mucosa. This interferes with healing. It occurs if the mucosa is pierced by the needle. Also the presence of suture material on the vesical side favours deposition of phosphate crystals, so we use inverting Lembert sutures.
4. The use of improper suture material. The suture material used should resist absorption for 30 days.

C. Causes after Operation

1. Obstruction of the catheter.
2. Occurrence of haemorrhage into the bladder leading to its distension. Treated by washing the bladder through the catheter with 1% silver nitrate solution.
3. Postoperative infection.

Treatment of Recurrent Vesicovaginal Fistula

The choice of operation depends upon several factors including the size and site of fistula, the extent of scarring, the number of previous operations, and the age of the patient. The alternative lines of treatment are:

1. Another vaginal repair.
2. Abdominal repair.
3. Colpocleisis. It is obliteration of the vagina and can be performed if the patient is postmenopausal or had hysterectomy. The vagina is closed below the level of the fistula.
4. Ileal conduit. It is implantation of ureters into an isolated loop of ileum which opens on the abdominal wall.
5. Ureterocolic implantation. Implantation of ureters into the sigmoid colon leads to ascending pyelonephritis and hyperchloraemic acidosis due to absorption of chloride and sodium ions from urine. It is restricted for malignant fistula.

Combined Vesicovaginal and Rectovaginal Fistulae

Both can be repaired in one sitting but there is no golden rule which one is closed first. Also one fistula may be closed first and the other one later on.

MENOURIA SYNDROME

This means amenorrhoea and cyclic haematuria due to the presence of a vesicouterine fistula. It may complicate lower segment caesarean section. Diagnosed by cystoscopy and hystero-graphy which will show the opening in the bladder and the fistulous tract from the uterus to the bladder. The accepted treatment is abdominal closure of the fistula. However, we may induce amenorrhoea by giving a combined contraceptive tablet daily for 6 months. This may be followed by spontaneous closure. If there is a breakthrough bleeding or blood stained urine, we increase the dose to 2 tablets daily. This syndrome was first described by Professor Yousef (Cairo University) in 1957.

Complications of Urinary Fistulas

1. Urinary tract infection, stone formation and renal failure.
2. Hydroureter and hydronephrosis due to ureteric stenosis caused by fibrosis at the site of the ureteric fistula.
3. Vulvitis, vaginitis, and formation of phosphatic deposits on the vulva.
4. Vaginal stenosis due to scarring. Stones may form in the vagina.
5. Psychological disturbances as amenorrhoea.

URETEROVAGINAL FISTULA

Aetiology

A. Congenital.

B. Traumatic

1. Obstetric trauma is a rare cause because the ureter is displaced upwards during labour.
2. Surgical trauma e.g. total hysterectomy which is the commonest cause of this type of fistula.
3. Direct trauma as fracture of pelvis or vaginal rupture.

C. Postirradiation e.g. application of radium for cervical carcinoma.

Diagnosis

1. Partial incontinence of urine.
2. Methylene blue test. The pieces of gauze will be soaked with urine.
3. Intravenous pyelography. The course of the affected ureter will be interrupted at the site of the fistula and its lower end may not be seen. There is also hydronephrosis.
4. Cystoscopy. The urinary efflux is weak or absent from the affected side. If we try to pass a ureteric catheter it will stop at the site of the fistula and cannot reach the renal pelvis. If we inject indigocarmine I.V. the coloured urine will be seen coming from the healthy ureter (4 ml 4% solution I.V., the violet colour appears after 4 minutes).

Treatment

Reimplantation of the ureter into the bladder or into a rolled bladder flap (Boari operation). This is done abdominally. If the fistula is high, the ureter is implanted into an isolated loop of ileum with one end opening on the abdominal wall (ileal conduit) or the ureter is implanted into the sigmoid colon. If the function of the kidney is greatly impaired, nephrectomy is performed.

Notes

- Ureterovaginal fistula leads to complete incontinence of urine when the lesion is bilateral or the kidney on the opposite side is absent or not functioning.
- Kidney function tests include: (1) urinalysis and specific gravity; (2) blood urea (20-40 mg%); (3) serum creatinine (0.6-1.2 mg%); (4) urea concentration test; (5) urea clearance test; (6) creatinine clearance test; (7) intravenous pyelogram.

RECTOVAGINAL FISTULA

Aetiology

A. Congenital. It is very rare.

B. Traumatic. Due to different types of trauma:

1. Obstetric trauma. (a) The commonest cause of a rectovaginal fistula is incomplete healing of a complete perineal tear (4th degree) occurring during labour, also the rectum may be included in a stitch during repair of a tear or episiotomy; (b) necrotic obstetric fistula due to obstructed labour causing prolonged compression, ischaemia and necrosis of the rectovaginal septum; (c) traumatic obstetric fistula caused by instruments as perforator or decapitation hook.
2. Surgical trauma. The rectum may be injured during operation as total hysterectomy or posterior colporrhaphy.
3. Direct trauma; as defloration injuries, falling on sharp objects, ulceration of a neglected pessary or foreign body.

C. Inflammatory

A pelvic abscess may open into the vagina and rectum. Tuberculosis, syphilis and bilharziasis of the vagina or rectum are rare causes.

D. Neoplastic

Malignant tumour of cervix, vagina or rectum. Cervical carcinoma rarely invades the rectum, as Douglas pouch intervenes between the cervix and rectum.

E. Postirradiation

Radium applied for the treatment of cancer of cervix or vagina may cause ischaemic necrosis and fistula.

Diagnosis

I. Symptoms

The symptoms depend upon the size of the fistula. If it is large, there is loss of voluntary control over the passage of faeces and flatus. If the fistula is small the patient may complain of involuntary escape of flatus and liquid stools. Irritation by faecal matter leads to secondary vulvitis, vaginitis and persistent vaginal discharge.

II. Signs

The condition is diagnosed by exposing the posterior vaginal wall in good light. A small fistula is diagnosed by doing a rectal examination, a rectovaginal examination or by passing a blunt probe in the fistulous tract. Injection of methylene blue solution into the rectum is sometimes required to find the opening of a very small fistula.

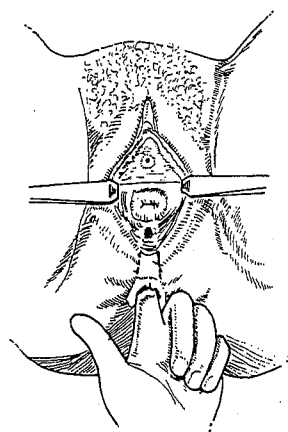


Fig. 33. Rectovaginal fistula

Treatment

1. In case of inflammatory or malignant fistula, the treatment is that of the cause.
2. In congenital and traumatic fistula, the treatment is closure of the fistula by operation. The preoperative and postoperative management are the same as in case of a complete perineal tear (page 83). The type of operation depends upon the site and size of the fistula.

i. Fistulae in the Lower Third of the Vagina

- a. Lawson Tait operation. Indicated when the fistula is large and the perineal body below the fistula is inadequate. We cut the bridge of tissue below the fistula converting it into a complete perineal tear which is then repaired in layers.
- b. Vernon-David operation. Indicated when the fistula is small and the perineal body is intact. A circular incision is made in the vaginal wall around the fistulous opening. The fistulous tract is then dissected and inverted into the rectum to undergo sloughing. The

opening in the rectal wall is closed, the levator ani muscles are approximated between the rectum and vagina, then the vagina is closed.

ii. Fistulae in the Middle Third

These are closed by the flap-splitting operation as that done for closing a vesicovaginal fistula.

iii. Fistulae in the Upper Third

These are closed abdominally. If the fistula is large a temporary colostomy is done 2 weeks before operation and then closed after healing of the fistula (at least 6 weeks after operation).

SECTION V

GENITAL DISPLACEMENTS

GENITAL PROLAPSE

DEFINITION

Prolapse means descent of a genital organ below its normal position.

TYPES

1. Uterine prolapse.
2. Vaginal prolapse.
3. Combined vaginal and uterine prolapse. This may be uterovaginal or vaginouterine.
4. Prolapse of the ovaries and tubes.

UTERINE PROLAPSE

DEGREES

First degree

The external os of the cervix descends below the level of the ischial spines when the patient stands or strains but it does not appear from the vagina.

Second degree

The cervix but not the whole uterus appears from the vagina on standing or straining (incomplete procidentia).

Third degree

The whole uterus is prolapsed outside the vagina. This is known as complete procidentia.

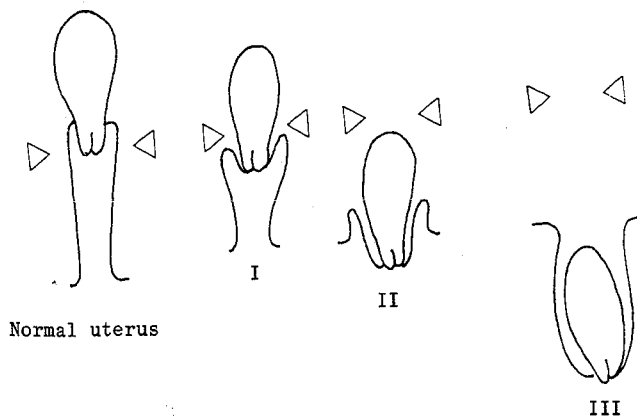


Fig.34. Degrees of uterine prolapse

VAGINAL PROLAPSE

1. PROLAPSE OF THE ANTERIOR VAGINAL WALL

- Descent of the upper two-thirds with the base of the bladder → cystocele.
- Descent of the lower third with the urethra → urethrocele.
- Descent of all the anterior vaginal wall → cystourethrocele.

2. PROLAPSE OF THE POSTERIOR VAGINAL WALL

- Descent of the upper third with the peritoneum of Douglas pouch containing loops of intestine → enterocele (hernia of Douglas pouch).
- Descent of the middle third with the underlying rectum → rectocele.
- Descent of the lower third with the underlying anal canal → rectocele.

3. VAULT PROLAPSE

It is descent of vaginal vault after hysterectomy.

FACTORS WHICH KEEP THE UTERUS AT ITS NORMAL POSITION

- The cervical ligaments.
- The pelvic floor muscles (levator ani and perineal muscles).
- The anteverted position of the uterus.

AETIOLOGY OF PROLAPSE

There are primary and secondary causes.

1. Primary (Predisposing) Causes

1. *Weakness of the Cervical Ligaments*

The causes are:

- Congenital weakness. This leads to appearance of prolapse at an early age, the so-called "virginal" or "nulliparous" prolapse. Congenital prolapse found at birth is rare. It is usually associated with spina bifida. The condition may be accompanied with generalised visceroptosis.
- Obstetric trauma. It is the commonest cause of prolapse. The factors responsible are: delivery of a large baby, straining during the first stage of labour before the cervix is fully dilated, forceps or breech extraction before the cervix is fully dilated, getting up early after labour and repeated deliveries at short intervals. This does not allow sufficient time for involution of the supporting ligaments.
- Postmenopausal atrophy. This may lead to appearance of prolapse after the menopause.

2. *Injury of the Pelvic Floor Muscles*

It is the result of childbirth. Unrepaired, badly repaired or hidden perineal tear predisposes to prolapse. Hidden perineal tear is due to overstretching or prolonged distension of the

perineum by fetal head causing laceration and weakness of the levator ani muscles although the skin of the perineum remains intact.

3. Retroversion of Uterus

The intra-abdominal pressure tends to push the uterus downwards when it becomes retroverted and lies along the axis of the vagina.

II. Secondary (Precipitating) Causes

These cause prolapse when a weakness is already present so they act as precipitating factors. Secondary causes include:

- a. Increased intra-abdominal pressure, due to chronic cough, chronic constipation, ascites, abdominal tumours and obesity.
- b. Increased weight of the uterus, due to early pregnancy, subinvolution and small fibroids. If the size of the uterus is large, it rests on the pelvic brim and will not prolapse.
- c. Traction on the uterus by a large cervical polyp or by vaginal prolapse.

ANATOMY AND COMPLICATIONS OF PROLAPSE

The Vagina

1) The vaginal wall becomes thickened due to congestion and oedema. 2) The mucosa loses its rugae and becomes smooth. 3) When the vaginal mucosa is exposed to air it may become dry and keratinized and areas of pigmentation may appear. 4) Trophic or decubital ulcer sometimes occurs on the vagina or portio vaginalis of the cervix. It is caused by: (a) congestion of the tissues leading to interference with nutrition (main cause); (b) friction with the thighs and clothes; (c) irritation by urine and faeces; (d) atrophy of vaginal mucosa occurring after the menopause.

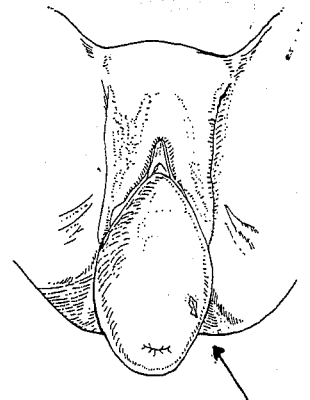


Fig. 35. Uterine prolapse with trophic ulcer

The Cervix

Descent of the cervix leads to: (1) Hypertrophy due to congestion and oedema; (chronic hypertrophic cervicitis); (2) elongation of the supravaginal portion because the upper part of the Mackenrodt ligament is strong and resists traction by the prolapsed vagina; (3) trophic ulcer may occur. Sometimes the prolapsed cervix and adjacent vaginal walls become congested and oedematous and cannot be reduced by the patient i.e. incarcerated.

The Body of Uterus

Descent of uterus leads to congestion of the endometrium. This leads to menorrhagia and increased normal vaginal discharge. In second and third degree uterine descent, the uterus is found retroverted.

The Tubes and Ovaries

These become prolapsed with the uterus. Prolapse of ovaries leads to dyspareunia and ovarian congestion. Congestion of the ovaries may cause polymenorrhoea.

The Urinary Tract

(a) In cystocele, there is descent of the base of the bladder leading to difficulty of micturition (dysuria). Sometimes, the patient cannot micturate unless she pushes up the cystocele with her finger in the vagina, (b) retention of urine causes infection and cystitis which leads to frequency and painful micturition, (c) stress incontinence may occur; (d) in second and third degrees of uterine prolapse the ureters become obstructed leading to hydronephrosis and hydronephrosis. As the uterus descends, the ureters which pass through the cardinal ligaments descend with it and become kinked.

Note. Stress incontinence occurs when the bladder neck descends below the pelvic floor, so with increased intra-abdominal pressure, the pressure will be transmitted to the bladder and not to the upper urethra leading to escape of urine.

DIAGNOSIS

A. Symptoms

Minor degrees of prolapse are asymptomatic, however, the patient may complain of one or more of the following:

1. A sensation of heaviness in the pelvis due to the presence of a swelling in the vagina.
2. A swelling which protrudes from the vulva on standing or straining and disappears when the patient lies down.
3. Low backache (sacralgia) due to pelvic congestion or stretching of the uterosacral ligaments by a uterine prolapse. It becomes progressively worse during the day and is relieved by lying down.
4. Pain in the groins due to traction on round ligaments.
5. Symptoms of pelvic congestion as congestive dysmenorrhoea, menorrhagia, polymenorrhoea (congestion of ovaries) and increased normal vaginal discharge (leucorrhoea). Trophic ulcer may cause a purulent or blood stained vaginal discharge.
6. Urinary symptoms may occur with a cystocele. (a) There is difficulty of micturition (dysuria). Sometimes the patient cannot micturate unless she pushes up the cystocele with her finger in the vagina; (b) retention of urine causes infection and cystitis which leads to frequency and painful micturition; (c) stress incontinence.
7. Rectal symptoms may occur with a rectocele. There is heaviness in the rectum and dyschezia. The patient may need to push the rectocele upwards by a finger in the vagina to be able to defaecate. Piles may develop due to straining.
8. Dyspareunia, due to the presence of a swelling in the vagina.
9. Infertility; due to congestion of endometrium preventing implantation of the ovum, backward displacement of uterus and dyspareunia.

Note. Symptoms of enterocele; (1) may be asymptomatic; (2) a sensation of heaviness in the pelvis; (3) vulval swelling; (4) low backache; (4) dyspareunia due to the presence of a swelling in the vagina.

B. Signs

1. General examination; mainly for chronic bronchitis and obesity which increase the intra-abdominal pressure. The back is examined for spina bifida and x-ray of lumbosacral area should be done in nulliparous prolapse.
2. Abdominal examination to exclude visceroptosis or a cause of increased intra-abdominal pressure as ascites. The kidneys are palpated for enlargement or tenderness.
3. Pelvic examination:
 - a. Inspection. The perineum is examined for lacerations. The patient is asked to cough or to strain down to know the type of prolapse and the presence of stress incontinence.
 - b. Digital palpation. To confirm the nature of the prolapsed mass. The levator ani muscles are palpated to determine their tone.
 - c. Bimanual examination. To detect retroversion or a pelvic mass. If supravaginal elongation is suspected we pass a uterine sound to know the length of the cervix.
 - d. Speculum examination; to exclude a lesion in the cervix. Prolapse is best examined by Sims speculum with the patient in the left lateral position.
 - e. Rectal examination; must be done to confirm the diagnosis of rectocele or enterocele.

Note. First degree uterine prolapse is diagnosed by vaginal examination when the cervix descends below level of ischial spines while the patient is straining.

TREATMENT

The treatment is prophylactic, palliative and surgical.

Prophylactic Treatment

1. During labour. Avoid the factors which predispose to prolapse as straining during the first stage of labour, forceps or breech extraction before the cervix is fully dilated, etc. Frequent emptying of the bladder, so that it is not pushed downward by the fetal head. Episiotomy when indicated to avoid overstretching and weakness of pelvic floor.
2. After labour. (a) Any perineal or vaginal tear must be sutured immediately after delivery; (b) pelvic floor exercises; (c) the patient is asked to lie on her abdomen for one hour daily to prevent retroversion which predisposes to prolapse; (d) treatment of puerperal constipation to avoid bearing down while supporting ligaments are lax; (e) if prolapse is detected during the puerperium, a ring pessary is applied for 3 months until the supporting ligaments involute and restore their tone; (f) proper spacing of pregnancies.
3. At hysterectomy. The stumps of the round, cardinal and uterosacral ligaments are sutured to the vault of the vagina to prevent its prolapse.

Note for the postgraduate

A simple pelvic floor exercise is to ask the patient to contract the levator ani repeatedly for 2 minutes twice daily over a number of months. Also Kegel perineometer can be used. A pneumatic tube is

inserted into the vagina, and the woman contracts the levator ani muscles to raise the pressure in the connected pressure gauge to the maximum.

Palliative or Pessary Treatment

A pessary does not cure uterine prolapse. It only keeps the uterus up and gives temporary relief of symptoms. A pessary is indicated in the following conditions:

1. Prolapse of uterus in early pregnancy. The pessary is applied till the 20th week when its size prevents its descent.
2. Prolapse detected in the puerperium.
3. Slight degree of prolapse (cystocele, rectocele, and uterine) in a young woman until she completes her family.
4. The presence of a contraindication to operation as advanced diabetes mellitus.
5. When the patient refuses operation.
6. To help the healing of a trophic ulcer.

The pessary used is either the ring or "cup and stem" pessary.

The Ring Pessary

It is made of rubber or plastic. A pessary of suitable size is introduced into the vagina above the level of the levator ani muscles. It stretches the vaginal walls and prevents descent of the uterus.

The "Cup and Stem" or Napier Pessary

It is used when the ring pessary cannot be retained in the vagina because the pelvic floor is weak or lacerated and when there is complete procidentia or congenital prolapse.

Precautions during Wearing a Pessary

1. A daily vaginal douche using normal saline.
2. Every month the pessary is removed, cleaned and the vagina is examined for inflammation or ulceration, then the pessary is reapplied.
3. The pessary stretches the tissues and after few months (4-6 months) a bigger size may be needed to control the prolapse.

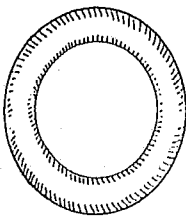


Fig. 36. Ring pessary

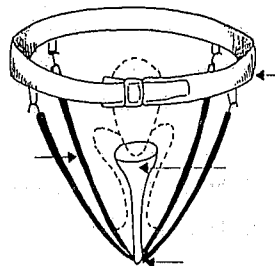


Fig. 37. Napier cup and stem pessary

Surgical Treatment

It is the curative treatment and indicated only if symptoms are present.

Preoperative Preparation

1. Blood picture with correction of anaemia and general health.
2. The urinary tract is investigated by urine analysis, culture and sensitivity test. Estimation of blood urea, serum creatinine, and intravenous pyelography are indicated in complete procidentia. Any urinary infection must be treated before operation.
3. Trophic ulcer on cervix or vagina is treated by putting a pack of gauze in the vagina soaked in flavine solution to reduce the prolapse to diminish congestion. This can also be done by inserting a ring pessary to elevate the uterus. Oestrogen may be given orally or locally as cream, especially in menopausal women to improve healing of vaginal epithelium. Ulcers slow to heal are painted with silver nitrate solution.
4. Operation is done in the postmenstrual week to minimize the blood loss and to allow healing to occur before next menstruation.

Note. Obese patient should reduce her weight before surgery to avoid raised intra-abdominal pressure and recurrence of prolapse.

Types of Operations

The choice of operation depends upon the type of prolapse and age of the patient.

A. Operations for patients in the childbearing period

1. Cystocele is treated by anterior colporrhaphy. However, some surgeons do posterior colpoperineorrhaphy as well, i.e. classical repair. The aim of the posterior repair is to strengthen the lax pelvic floor to prevent recurrence.
2. Rectocele is treated by posterior colpoperineorrhaphy.
3. Combined vaginal and uterine prolapse is treated by Fothergill (Manchester) operation or its modification, i.e. without amputation of the cervix.

Anterior Colporrhaphy

The anterior vaginal wall is separated from the bladder. The bladder is pushed upwards to its original position as a pelvic organ behind the symphysis pubis. The fascia between the bladder and vagina is sutured in the midline to form a shelf below the bladder. Redundant vaginal wall is removed and the vagina is closed in the midline. Chromic catgut or delayed-absorbable sutures as Vicryl are used for repair. A Foley catheter and a tight vaginal pack are usually inserted and left for 24 hours. The pack helps haemostasis and prevents reactionary haemorrhage.

Note. The fascia between the bladder and vagina is difficult to identify and it has various names: pubovesical fascia, pubocervical ligaments or fascia of Denonvilliers.

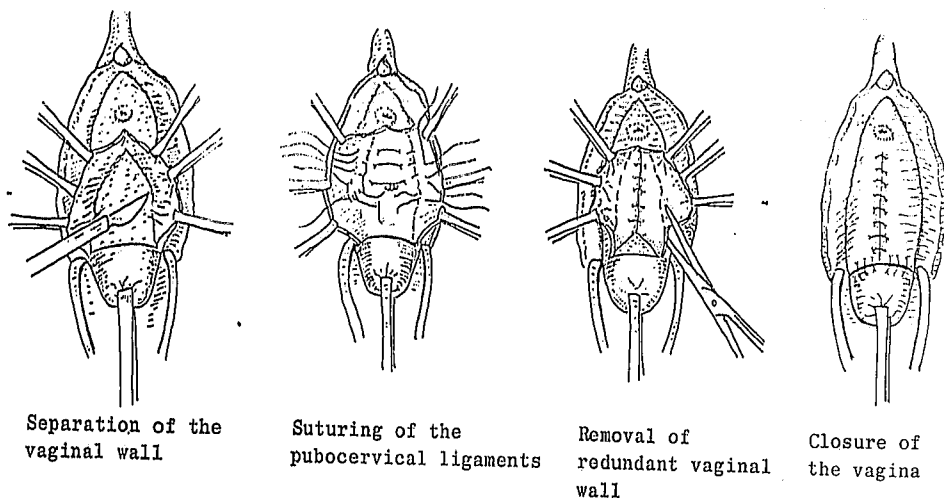


Fig. 38. Anterior colporrhaphy.

Posterior Colpoperineorrhaphy

The posterior vaginal wall is separated from the rectum. The two levator ani muscles are approximated in the midline in front of the rectum. Redundant vaginal wall is removed and the vagina is closed. The superficial perineal muscles are sutured together in the midline and the skin is closed. Finally, a Foley catheter and a tight vaginal pack are usually inserted and left for 24 hours.

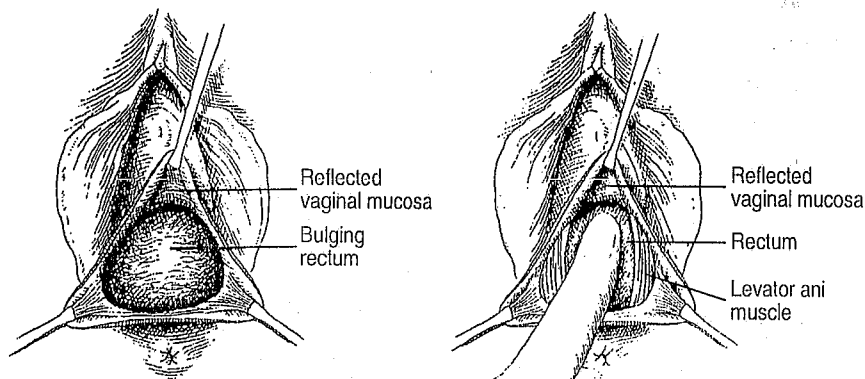


Fig. 38-2. Posterior colpoperineorrhaphy.

Fothergill (Manchester) Operation

It is indicated for combined vaginal and uterine prolapse when there is supravaginal elongation of the cervix or when it is lacerated or infected. It consists of 7 steps:

1. A uterine sound is passed to measure the length of cervix to estimate the length to be amputated.
2. Dilatation and curettage. Dilatation is necessary to allow covering the raw area left after amputating the cervix. Curettage to remove the congested endometrium, to reduce the amount of subsequent menstruation, and to exclude any endometrial pathology.

3. Anterior colporrhaphy to correct the cystocele.
4. Amputation of the cervix to restore its normal length which is one inch.
5. The Mackenrodt ligaments are sutured together in front of the cervix. This shortens the ligaments and elevates the uterus upwards, also the cervix is pulled backwards to correct retroversion.
6. The raw area of the cervical stump is covered by mucosa.
7. Posterior colpoperineorrhaphy is then performed.

If the cervix is not elongated, infected or lacerated the case is treated by modified Fothergill operation that is without amputation of the cervix (anterior repair + suturing of Mackenrodt ligaments in front of cervix + posterior repair).

Complications

1. The operation takes a long time.
2. There is excessive blood loss throughout the operation.
3. Injury of urinary bladder, ureter or rectum.
4. High amputation of the cervix may lead to abortion or recurrent preterm labour due to cervical incompetence.
5. Subsequent fibrosis in the cervix may lead to infertility, dysmenorrhoea, haematometra or failure of the cervix to dilate during labour (cervical dystocia).
6. Dyspareunia due to narrowing of the vagina or tender scar.

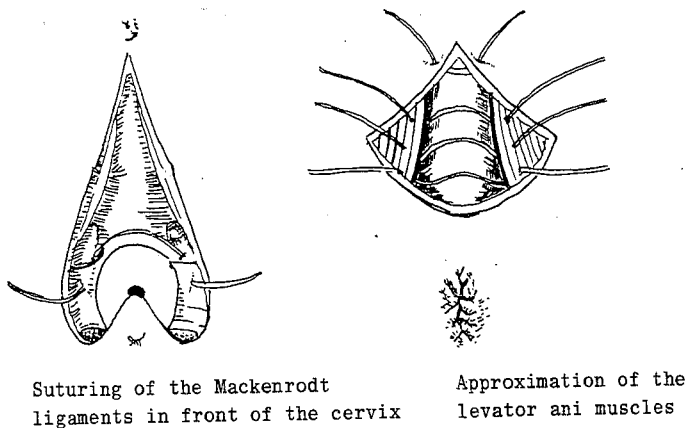


Fig. 39. Fothergill operation

B. Operations for Patients after the Menopause

1. Anterior colporrhaphy for cystocele.
2. Posterior colpoperineorrhaphy for rectocele.
3. Vaginal hysterectomy with anterior and posterior repair. Indicated for second and third degree uterine prolapse in a patient after the menopause. Also indicated in a patient near menopause when prolapse is associated with uterine pathology needing hysterectomy as metropathia haemorrhagica or small fibroids.

4. Le Fort operation. A rectangular area is removed from the anterior vaginal wall and a similar flap is removed from the posterior wall. The 2 raw areas are sutured together closing the vagina but leaving 2 small channels on either side to allow drainage of any cervical discharge. The operation takes little time and can be done under local anaesthesia. It is indicated for uterine prolapse in a postmenopausal unmarried woman whose general condition cannot tolerate another operation.

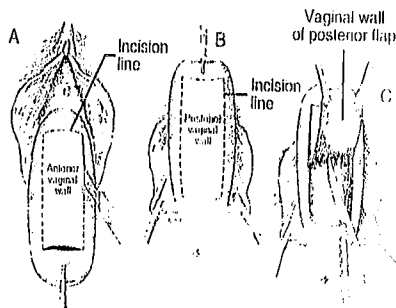


Fig. 39-2. Le Fort operation.

C. Other Types of Operations

1- Sling Operations

Used for congenital uterine and vault prolapse. Non-absorbable material as nylon tape is used to suspend the cervix or vault of vagina to the periosteum of the sacrum or rectus sheath. Vault prolapse can also be treated by fixing the vaginal vault to the sacrospinous ligament on one side (transvaginal sacrospinous colpopexy).

2- Operations for Hernia of Douglas Pouch

- a. Vaginal repair. The posterior vaginal wall is dissected upwards till the posterior fornix. The hernial sac is dissected and opened. The contents are displaced. The neck of the sac is transfixed and ligated and the sac is excised. The uterosacral ligaments are sutured together. Posterior repair is then performed.
- b. Abdominal repair. The Douglas pouch is obliterated by a series of purse string sutures from below upwards using delayed-absorbable sutures as Vicryl. The needle bites include the uterosacral ligaments, the posterior wall of cervix and the serous coat of the rectum (Moschowitz operation). In Halban operation 5 or 6 stitches are passed in the peritoneum of Douglas pouch from before backwards to obliterate the pouch. This avoids the uterosacral ligaments to avoid injury of ureters. Abdominal repair is used if laparotomy is done for another purpose.

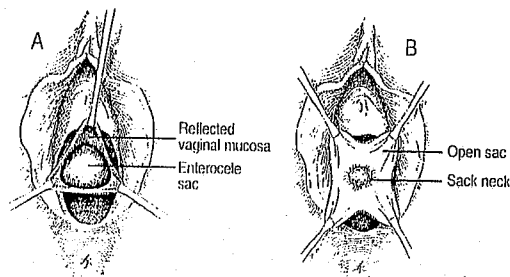


Fig. 39-3. Repair of enterocele.

Note. It is preferable not to treat prolapse until the patient completes her family as vaginal delivery may lead to recurrence of the prolapse.

THE DIFFERENTIAL DIAGNOSIS OF A MASS PROTRUDING FROM THE VULVA

A. From the Anterior Vaginal Wall

1. **Cystocele.** Appears on standing or straining. It is reducible (can be moved from its position) and compressible. If a catheter is passed it can be felt in the mass.
2. **Cyst of the anterior vaginal wall.** The commonest is Gartner cyst which is derived from Gartner or Wolffian duct. It is irreducible, incompressible, usually lateral to the midline and may be multiple. If a catheter is passed it will show a normal direction of the urethra anterior to the cyst.
3. **Urethral or bladder diverticulum.** It is compressible. Pressure on a urethral diverticulum will cause escape of urine or pus from the external meatus. Urethroscope or cystoscope will show the opening of diverticulum.

B. From the Posterior Vaginal Wall

1. **Rectocele.** Appears on standing or straining, reducible and compressible. A finger in the anus will pass into the mass.
2. **Enterocele or hernia of Douglas pouch.** (a) There is descent of the upper part of posterior vaginal wall; (b) an impulse on cough may be seen or felt; (c) gurgling of the intestine may be detected on palpating the mass; (d) rectal examination shows that the rectum is pushed backwards by the swelling and is not forming part of it; (e) enterocele can be detected by performing a combined rectovaginal examination while the patient is standing. This allows palpation of the small bowel between the thumb in the vagina and index finger in the rectum (Malpus test).
3. **Cyst of the posterior vaginal wall, as dermoid cyst.** It is irreducible and incompressible. A finger in the anus will not pass into the mass.

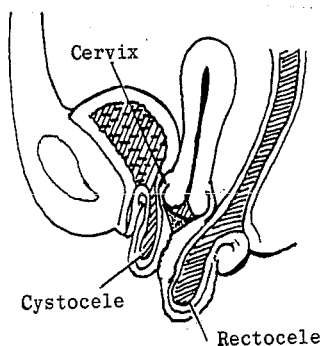


Fig.40. Cystorectocele

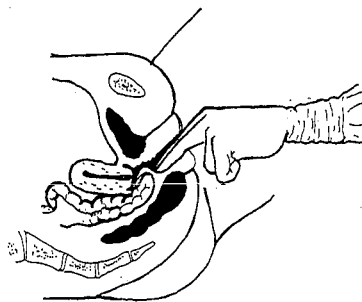


Fig.41. Enterocele

C. From the Uterus

1. **Second and third degree uterine prolapse.** The external os appears from the vagina. In second degree the elongated supravaginal cervix is felt as a thick cord and this can be confirmed by passing a uterine sound. In third degree the thumb and index finger can meet together above the fundus of uterus when the uppermost portion of the prolapsed mass is palpated (finger test or grip sign).
2. **Congenital elongation of the cervix.** The vaginal vault is at its normal level i.e. above the level of ischial spines. The cervix is low in the vagina or even outside the vagina. It is due to elongation of the vaginal and not the supravaginal part of the cervix as shown by the uterine sound. This condition is called false prolapse. Treated by amputating the elongated portio vaginalis leaving a normal length of the cervix.
3. **Fibroid polyp.** (a) Absence of external os; (b) the cervix is at its normal position with the pedicle of the tumour coming out through the cervix; (c) a sound can be introduced for a long distance in the uterine cavity.
4. **Inversion of uterus.** (a) Absence of external os; (b) the mass is covered by smooth endometrium; (c) the body of the uterus is not felt per abdomen; (d) a uterine sound can be introduced for a short distance or cannot be introduced at all.
5. **A cauliflower carcinoma or sarcoma of cervix or vagina** may appear at the vulva. The mass is friable, necrotic, indurated at the base and bleeds on touch.



Fig.42. Congenital elongation of cervix



Fig.43. Fibroid polyp

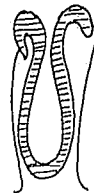


Fig.44. Inversion of uterus

RECURRENT PROLAPSE

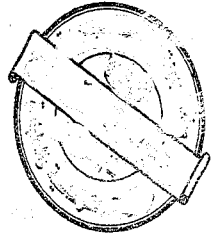
AETIOLOGY

- A. **Causes before operation.** (1) Congenital weakness of the cervical ligaments; (2) bad general health and anaemia; (3) the presence of infection or ulceration in the cervix or vagina; (4) if the factors which increase the intra-abdominal pressure as chronic cough, chronic constipation, and obesity are not corrected before operation.

B. Causes during operation. (1) Poor surgical techniques; (2) bad choice of operation, e.g., vaginal repair for a congenital uterine prolapse; (3) missing a hernia of Douglas pouch (commonest cause); (4) an elongated cervix which was not amputated; (5) shortening of the vaginal wall, so the cervix becomes near to the vaginal orifice; (6) failure to support the vaginal vault after hysterectomy leading to vault prolapse; (7) use of early-absorbable sutures leads to recurrence.

C. Causes after operation. (1) Infection; (2) early ambulation; (3) early subsequent pregnancy; (4) repeated deliveries; (5) if episiotomy is not done at the time of subsequent delivery; (6) postmenopausal atrophic changes.

The rate of recurrence is about 7%.



Clinical Picture

1. History of previous operation for repair of prolapse.
2. Presence of symptoms which depend upon the type of prolapse.
3. Examination reveals the nature of prolapse, and scar of previous operation.
4. The cause of recurrence has to be determined as chronic cough and obesity.

Treatment

1. Treat the cause of recurrence.
2. The operation depends upon the type of prolapse and the general condition of the patient.
3. Operation is done at least 3-6 months after the previous repair to allow absorption of scar tissue. Fibrous tissue resulting from the previous operation makes the second operation more difficult.

ANATOMY OF ANTERIOR VAGINAL WALL

(1) On either side of the urethral meatus, there is a depression called paramental recess; (2) the submental sulcus is 0.6 cm. from the urethral meatus; (3) the transverse vaginal sulcus is a transverse groove 3-4 cm. from the urethral meatus, it is at the junction of the urethra with the bladder neck and at which the vesical and vaginal fasciae fuse together; (4) the bladder sulcus at the level of the fundus of the bladder.

Note. In urethrocele there is descent of the anterior vaginal wall between the submental and transverse vaginal sulcus and in cystocele there is descent between the transverse vaginal sulcus and bladder sulcus.

Relationship between Uterine Prolapse and Cervical Carcinoma

Third degree uterine prolapse (complete procidentia) predisposes to vaginal carcinoma. However, it is very rare to find cervical carcinoma in association with complete procidentia. This may be explained by:

1. Congestion of the cervix and keratinization of the covering cervical epithelium may raise the resistance to cancer.

2. The prolapsed cervix is not bathed in any infected or irritating vaginal discharge.
3. The presence of the cervix outside the vagina decreases its temperature. It is known that the undescended testicles which lie in a warm place inside the body are more liable to develop cancer.
4. Infiltration of the parametrium in case of cervical carcinoma fixes the uterus and prevents its descent.

RETROVERSION AND RETROFLEXION

Normally, the uterus is anteverted anteflexed. In about 15% of normal women it is retroverted or retroflexed or both i.e. retroversion-flexion or R.V.F.

AETIOLOGY

A. Developmental (15%)

In this case the uterus may be normal in size or hypoplastic.

B. Acquired

1. **Puerperal retroversion.** Occurring after abortion or labour and it is the commonest cause of acquired retroversion. The predisposing factors are: (a) laxity of the supporting ligaments of the uterus allowing it to rotate backwards; (b) increased bulk and weight of the body of the uterus while the lower segment is soft; (c) persistent distension of the bladder during puerperium thus pushing the uterus backwards; (d) prolonged stay in bed with the patient lying in the dorsal position (effect of gravity).
2. **Pelvic lesions.** A tumour lying in front of the uterus pushes it backwards. The uterus may be pulled backwards by adhesions as in cases of endometriosis and chronic salpingo-oophoritis.
3. **Prolapse.** As the uterus descends it lies along the axis of the vagina so it becomes retroverted. So retroversion predisposes to prolapse or when the uterus descends it becomes retroverted.

Note. The uterosacral ligaments are the cervical ligaments which keep the uterus anteverted.

DEGREES OF R.V.F.

First degree. The fundus of the uterus is directed towards the promontory of sacrum.

Second degree. The fundus is directed towards the sacral concavity.

Third degree. The fundus is directed towards the tip of sacrum.

TYPES

The retroverted uterus may be mobile or fixed.

DIAGNOSIS

Symptoms

In about 50% of cases, the symptoms are absent and the condition is discovered accidentally. However, the patient may complain of one or more of the following:

- A. Symptoms related to pelvic congestion as congestive dysmenorrhoea, menorrhagia, polymenorrhoea (congestion of ovaries) and increased normal vaginal discharge (leucorrhoea).
- B. Symptoms related to the abnormal position of uterus:
 1. Low backache; due to pressure of uterus on the uterosacral ligaments and pelvic congestion.
 2. Spasmodic dysmenorrhoea.
 3. Dyspareunia, due to prolapse of ovaries in Douglas pouch and direct pressure on the uterus itself.
 4. Infertility. This may be due to: (a) the cervix is directed forwards away from the seminal pool in the posterior fornix; (b) kinking of the cervical canal due to acute retroflexion; (c) congestion of the endometrium interfering with implantation of the ovum or causing early abortion; (d) hypoplasia of uterus present in some cases; (e) kinking of the tubes; (f) pelvic adhesions which resulted in fixed retroversion; (g) dyspareunia may prevent proper sexual intercourse. Infertility is present in 25% of cases.
 5. Complications may occur during pregnancy as abortion, incarceration, or anterior sacculation.

Note. When the uterine vessels reach the internal cervical os, they change their direction and run backward and downward along the side wall of the uterus. This leads to kinking of the thin-walled veins and not the arteries. The result is congestion of the uterus, tubes, ovaries, and broad ligaments (pelvic congestion).

Signs

The condition is diagnosed by vaginal examination which will show:

1. The posterior lip of the cervix will be felt at first and not the anterior lip.
2. The external os is directed downwards and forwards or even directly forwards (downwards and backwards in anteversion).
3. On bimanual examination the body of the uterus is not felt through the anterior fornix but through the posterior fornix.
4. The tubes and ovaries are frequently prolapsed in Douglas pouch. The ovaries will be felt as round, mobile, usually tender bodies.
5. The uterine sound can be used to confirm the diagnosis if palpation is difficult as in case of obesity. Also sonography diagnoses the case.

The Pessary Test

It is done before any surgical treatment to be sure that the symptoms are due to retroversion and so will be cured by operation. The uterus is corrected and a Hodge pessary is inserted to keep it anteverted. The patient is examined after one month, if symptoms persist, they are due to some other cause. If symptoms disappear but reappear after removal of the pessary, then RVF is the cause and operation can be performed.

Treatment

The treatment is prophylactic, palliative and surgical.

Prophylactic Treatment

This is carried out after labour and includes: (1) frequent emptying of the bladder as a full bladder pushes the uterus backwards; (2) pelvic floor exercises; (3) the patient is asked to lie on her abdomen for one hour daily to encourage anteversion; (4) if the uterus is found retroverted during the puerperium, it should be corrected and a Hodge pessary is inserted for 3 months.

Palliative or Pessary Treatment

The uterus is corrected at first and then a Hodge or Smith pessary is introduced to keep it anteverted. The pessary is made of plastic or vulcanite. The pessary stretches the posterior fornix and the overlying uterosacral ligaments thus the cervix is pulled backwards and the uterus is kept anteverted. Also the pessary narrows Douglas pouch, which will not accommodate the uterus if it falls backwards. The indications of pessary are:

1. Early pregnancy if retroversion has caused repeated abortions. The pessary is applied till the 14th week.
2. Retroversion detected in the puerperium.
3. As a pessary test before doing operation for retroversion.
4. Certain cases of infertility when other causes are excluded. The pessary does not interfere seriously with coitus.
5. The presence of a contraindication to operation as advanced diabetes mellitus.
6. When the patient refuses operation.



Fig. 45. Hodge pessary. The anterior and posterior ends are of the same diameter.

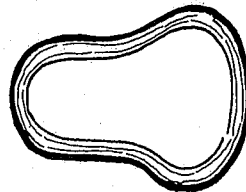


Fig. 46. Smith pessary. The anterior end which lies behind the symphysis pubis is narrower than the posterior end which lies in the posterior fornix.

Surgical Treatment

Indicated only if symptoms are present. Retroversion without symptoms requires no treatment. The main indication for surgical treatment is dyspareunia caused by prolapse of ovaries in Douglas pouch. Also operation is done as an added step to another operation as myomectomy

Types of Operations

Many operations have been described. The following are the commonest:

1. Modified Gilliam operation, the operation of choice. Laparotomy is done, and the round ligaments are shortened by their fixation to the anterior rectus sheath.
2. Retroversion with uterine prolapse is corrected by suturing the Mackenrodt ligaments in front of the cervix. See Fothergill operation.
3. Operations done as an added step to another operation as myomectomy to keep the uterus anteverted; (a) plication of round ligaments; (b) plication of uterosacral ligaments.

Notes for the postgraduate

1. In case of infertility, the patient is asked to have intercourse in the knee-chest position, so semen is deposited in the anterior fornix near the external os. Also a pessary can be inserted to keep the uterus anteverted. It does not interfere seriously with coitus.
2. Manual correction of retroversion. Lithotomy position. The index and middle fingers are inserted into the posterior vaginal fornix to push the body of the uterus upward and forward until it is felt by the abdominal hand which moves it forward, and the vaginal fingers are now placed into the anterior fornix to push the cervix backwards. In difficult cases, the trial is done with the patient in the knee-chest position or under anaesthesia. After correction, the pessary is inserted immediately. Also the pessary can be used to correct the uterus. Its upper broad end is carried on the index and middle fingers and placed in the vagina in front of the cervix. The cervix is pushed backwards until the end of the pessary slips and lies into the posterior vaginal fornix. The fingers then push the lower end of the pessary upward to be behind the symphysis pubis.

INVERSION OF UTERUS

The uterus is turned inside out. It may be acute or chronic.

ACUTE INVERSION

It occurs during or immediately after delivery of the fetus. It is called acute puerperal inversion and is discussed in obstetrics.

CHRONIC INVERSION

There is gradual prolapse of the uterine fundus through the dilated cervix. It is not accompanied by acute symptoms.

AETIOLOGY

1. **Chronic puerperal inversion.** It is the result of acute puerperal inversion which was not recognized at labour.

2. **Fundal tumour.** This may be a submucous myoma, fibroid polyp or malignant tumour.
3. **Senile inversion.** It occurs in old age due to cervical and uterine atony.

DEGREES

1. First degree. The fundus is depressed, so that it bulges into the uterine cavity "cupping of the fundus".
2. Second degree. The inverted fundus protrudes through the dilated cervix into the vagina.
3. Third degree. The inverted fundus appears at or protrudes through the vaginal introitus.

The first and second degrees are incomplete inversion, while the third degree is called complete inversion.

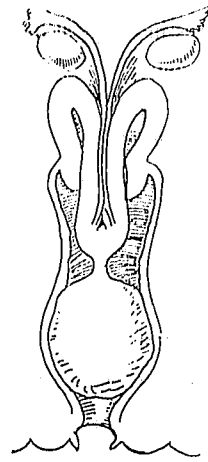


Fig.47. Myoma causing inversion

SYMPTOMS

1. Contact or irregular vaginal bleeding due to ulceration of the endometrium.
2. Vaginal discharge.
3. Chronic pelvic pain due to the presence of the tubes and ovaries in the uterine cup.
4. Dyspareunia caused by the presence of a mass in the vagina.
5. Infertility because of dyspareunia and infected endometrium.
6. Mass protruding from the vulva.

SIGNS

1. Abdominal examination. In the first and second degrees, cupping of the fundus is felt. In the third degree, the uterus is not felt per abdomen.
2. Vaginal examination. In the second and third degrees, there is a large mass in the vagina covered by dark red infected endometrium. A sound cannot be passed through the cervix or is introduced for a short distance.

DIFFERENTIAL DIAGNOSIS

1. A mass protruding in the vagina, such as uterine prolapse, cauliflower carcinoma or sarcoma arising from cervix or vagina.
2. Fibroid polyp protruding through the cervix. This is differentiated by:
 - a. Abdominal examination. In case of fibroid polyp, the uterus is felt per abdomen, and may be larger than normal due to associated fibroids.
 - b. Vaginal examination. In case of a polyp the uterine sound can be introduced for a long distance through the cervix.

TREATMENT

I. Senile inversion is treated by hysterectomy.

II. Inversion due to a fundal tumour:

1. Fundal myoma. If the woman is above 40 years hysterectomy is performed. If the patient is young, vaginal myomectomy is done and the inversion is corrected.
2. Malignant tumour. The treatment is according to the malignant condition.

III. Chronic puerperal inversion:

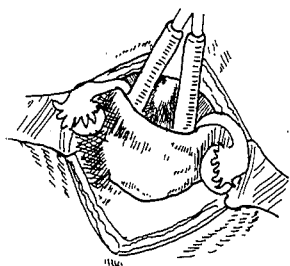
1. Surgical treatment:

a. Abdominal operations:

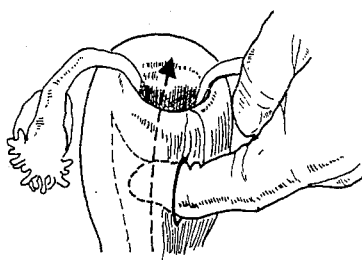
- i. Traction on the depressed fundus by a vulsellum (Huntington operation).
- ii. Division of the cervical ring anteriorly (Dobbin) or posteriorly (Haultain) and pulling on the fundus by a vulsellum to correct the inversion. A combination of traction and vaginal manipulation helps correction. The uterine incision is then closed. Posterior incision is preferred as anterior incision may extend into the bladder.
- iii. Abdominal hysterectomy. If the patient is above 40 years. Also indicated in case of sepsis or gangrene.

b. Vaginal operations:

- i. Division of the cervical ring anteriorly (Spinelli) or posteriorly (Kustner) followed by correction of the inversion and closure of the uterine incision.
 - ii. Vaginal hysterectomy. If the patient is above 40 years. Also indicated in case of sepsis or gangrene.
2. Conservative treatment by applying continuous pressure to correct the inverted uterus using the Aveling-S-shaped repositor. It is tried if the patient is unfit for surgery.



The cervical ring is stretched.



The ring is divided and a finger passed into the vagina hooks up the inverted uterus.

Fig. 48. Abdominal correction of inversion

Notes

- ... The Aveling-S-shaped repositor. The cup is applied to the inverted fundus. The stem is attached by rubber bands to an abdominal belt which is supported from the shoulders by straps.
- When the cervical ring is divided, cervical cerclage is necessary in a subsequent pregnancy, to prevent abortion or preterm labour, due to cervical incompetence.

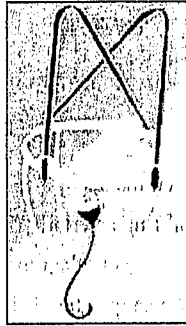


Fig. 48-2. Aveling repositor.

SECTION VI

GENITAL INFECTIONS

The female genital tract forms an open pathway between the exterior and the peritoneal cavity, so a defence mechanism must be present to prevent ascent of infection.

DEFENCE MECHANISM

(1) The vagina is mechanically closed by approximation of the labia and its anterior and posterior walls; (2) the vagina is lined by thick stratified squamous epithelium which does not contain glands, and is difficult to be invaded by bacteria; (3) the reaction of the vagina is acidic and this destroys most pathogenic organisms; (4) the cervix is closed by a mucous plug which is also bacteriolytic; (5) the superficial layer of endometrium is shed every month during menstruation thus avoiding persistence of infection; (6) the movement of cilia in the uterus and tubes is in a downward direction.

The defence mechanism is interfered with in the following conditions: (1) before puberty and after menopause because the vagina is lined by thin epithelium, its acidic reaction is low (pH 6-8) and the endometrium does not undergo shedding; (2) during menstruation when the cervical plug is expelled and the vaginal acidity is lowered by the alkaline menstrual blood; (3) after abortion or labour as the cervix is dilated, the presence of a raw placental area and alkaline lochia diminishing vaginal acidity; (4) broad spectrum antibiotic therapy destroys other bacteria in the vagina and allows the growth of *Candida* organisms; (5) the use of combined contraceptive tablets stimulates the growth of *Candida* organisms. This applies to the high – but not to the low-dose oestrogen pills; (6) the tail of the intrauterine contraceptive device may favour the growth of anaerobic bacteria leading to bacterial vaginosis, and may also lead to ascending infection and salpingitis in 1-2% of cases; (7) vaginal douching which is a habit among some Egyptian women may reduce vaginal acidity, and allow introduction of pathogenic bacteria, carried by the fingers or equipment used predisposing to pelvic infection.

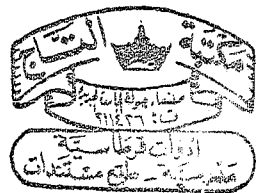
VULVITIS

Inflammation of the vulva may be primary or secondary.

PRIMARY VULVITIS

1. Skin Diseases

The skin of the vulva may be affected by any primary skin disease as tinea cruris, candidiasis, furunculosis, scabies, and eczema.



2. Sexually Transmitted Diseases

- a. Gonorrhoea. Gonorrhoeal vulvovaginitis may occur in children. In adult, the gonorrhoeal infection in the vulva is limited to the urethra and Bartholin gland.
- b. Syphilis. The vulva may be affected by chancre of primary syphilis, condylomata lata of secondary syphilis or gumma of tertiary syphilis.
- c. Soft sore.
- d. Granuloma venereum.
- e. Lymphogranuloma venereum.
- f. Genital herpes.
- g. Condylomata acuminata (genital warts).
- h. Molluscum contagiosum (viral infection). Infection by direct contact or by infected towelling, clothing, etc.

3. Chronic Specific Diseases

(a) Bilharziasis; (b) tuberculosis; (c) elephantiasis; (d) actinomycosis.

SECONDARY VULVITIS

The vulva may be irritated and inflamed secondary to:

1. Urinary Conditions

- a. Incontinence as in urinary fistula.
- b. Pyuria.
- c. Glycosuria as in diabetic cases.
- d. Severe frequency of micturition.

2, Vaginal Conditions

- a. Vaginal discharge, particularly due to monilia and trichomonas infection.
- b. Menorrhagia and polymenorrhoea.

3. Rectal Conditions

- a. Incontinence as in faecal fistula and complete perineal tear.
- b. Anal fistula.
- c. Oxyuris infection, particularly in children.

DIAGNOSIS OF VULVITIS

Most cases can be diagnosed by inspection in good light. We must do vaginal, bimanual and speculum examination in every case. Any discharge is examined bacteriologically. Skin biopsy of the vulva may be needed in obscure conditions as leucoplakia. In suppurative conditions and in the presence of moniliasis we have to exclude diabetes mellitus.

TREATMENT OF VULVITIS

1. Treatment of the cause.
2. General treatment:
 - a. Sedatives, as phenobarbitone, especially at night to prevent scratching.
 - b. Antihistaminics to prevent scratching.
 - c. In vulvitis of children and postmenopausal patients oestrogens can be given by mouth or locally to improve the vascularity and resistance of the vulva.
 - d. The underclothes should be of cotton (avoid nylon underwear).
3. Local treatment:
 - a. Local cleanliness. The vulva is shaved and washed several times daily with 1% sodium bicarbonate solution (soothing agent).
 - b. Antipruritic agents as cortisone, antihistaminic and anaesthetic ointments.

DIABETIC VULVITIS

It is the result of glycosuria which leads to chemical irritation. The condition is usually complicated by monilia infection because the fungus flourishes in the presence of sugar. The main symptom is pruritus which is exaggerated by the presence of peripheral neuritis. Diabetic vulvitis is characterised by: (1) severe itching. Pruritus vulvae may be the first symptom in diabetic cases; (2) inflammation is widespread and may extend to the skin of the thigh; (3) the skin is thickened and gray in colour due to scab formation; (4) furunculosis and ulcers may form as a result of scratching.

Treatment

(1) Control of diabetes; (2) treatment of associated monilia infection; (3) general and local treatment of vulvitis as mentioned before.

VAGINITIS

Inflammation of the vagina may be primary or secondary.

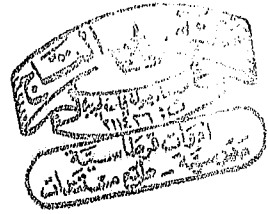
PRIMARY VAGINITIS

1. Vulvovaginitis of children.
2. Senile vaginitis.
3. Trichomonas vaginitis.
4. Candida (monilial) vaginitis.
5. Bacterial vaginosis.
6. Vaginitis emphysematosa.
7. Nonspecific vaginitis.
8. Cytolytic vaginitis.
9. Other types of vaginitis due to syphilis, bilharziasis, tuberculosis and diphtheria may occur.

SECONDARY VAGINITIS

The vagina may become irritated and inflamed secondary to:

1. Urinary conditions as urinary fistula, e.g. ureterovaginal and vesicovaginal fistula.
2. Rectal conditions as rectovaginal fistula and complete perineal tear.
3. Infected cervical discharge.
4. Mechanical irritation by a neglected pessary or foreign body.
5. Chemical irritation due to douching with irritating medications.
6. Application of radium for malignant disease of cervix or vagina.



VULVOVAGINITIS OF CHILDREN

The commonest age is 1-5 years. The infection occurs because the vulval and vaginal resistance are low due to lack of oestrogen and so liable to recur till puberty starts. This low resistance allows growth of pathogenic organisms, carried to the area by hands or dirty clothes.

Causative Organism

Any pathogenic organism as the streptococcus, staphylococcus, gonococcus, *Trichomonas vaginalis* or *Candida* may be responsible. Thread worms (*oxyuris vermicularis*), migrating from the rectum, may be a causative factor. Rarely, the condition is diphtheritic.

Mode of Infection

1. Organisms are transmitted from a child or adult by hands or clothes.
2. Sometimes a foreign body as pin is inserted by the child into the vagina causing infection.
3. Wiping of the perineum from anus to vagina may transfer enteric organisms, *Trichomonas vaginalis*, and *Candida* to the vagina.
4. A child with otitis media or tonsillitis may transmit bacteria by hand to the vulvovaginal area.
5. Sexual abuse leading to any sexually transmitted disease as gonorrhoea and *Trichomonas vaginitis*.
6. Local irritants may inflame the vulval tissues as nylon underclothes and harsh soaps.

Diagnosis

Symptoms

1. Purulent vaginal discharge. It may be blood stained if there is a foreign body, a cervical polyp, bilharzial papillomata, or the rare sarcoma botryoides.
2. Pain and soreness of the vulva secondary to irritation by vaginal discharge.
3. Pruritus vulvae.
4. Frequency and burning micturition due to irritation of the urethral meatus.

Signs

The vulva is inflamed, red, tender, sometimes oedematous or excoriated, and bathed in discharge. The labia minora may stick together, but can be easily separated apart leaving inflamed red surfaces.

Investigations

1. The discharge is examined by wet smear, Gram stained film, culture and sensitivity test.
2. The presence of a foreign body can be excluded by rectal examination, X-ray examination, sonography, or examination under general anaesthesia using a nasal speculum, a baby laryngoscope, a vaginoscope, or urethroscope.
3. Recurrent cases need stool examination for thread worms.

Treatment

1. A specific antibiotic is given according to the nature of the organism.
2. In nonspecific vaginitis an oestrogen cream is applied to the vulva each night for about 2 weeks. It increases local resistance to infection and relieves soreness.
3. Any foreign body must be removed.
4. Sedatives as phenobarbitone especially at night to prevent scratching.
5. Local washes with warm water and if the vulva is excoriated the child is kept at rest and adhesion of the labia is prevented by application of zinc oxide cream.
6. Boiling of the underclothes which should be of cotton.
7. Isolation from other children to prevent cross infection.

SENILE (ATROPHIC) VAGINITIS

After menopause (natural or artificial) the vaginal epithelium becomes thin and atrophic and the vaginal acidity is lowered, pH becomes 6-8. This is due to deficiency of oestrogen. These factors predispose to vaginitis by allowing growth of organisms which are normally inhibited by the protective mechanism. Senile endometritis is sometimes present as well.

Diagnosis

Symptoms

1. A postmenopausal purulent, sometimes blood stained vaginal discharge.
2. Pain and soreness of the vulva secondary to irritation by vaginal discharge.
3. Pruritus vulvae may be present.
4. Dyspareunia due to tenderness of the vagina.
5. Frequency and burning micturition due to irritation of the urethral meatus.

Signs

1. The vulva may be inflamed, red and tender.

2. The vaginal mucosa is thin, atrophic with absent rugae. It shows areas of ulceration which appear as bright red spots that bleed on touch. The raw areas may become adherent forming adhesions (adhesive vaginitis).

Treatment

1. Oestrogen is given orally or locally to increase vaginal resistance. A Premarin tablet (0.625 mg) is taken daily for 3 weeks or Premarin cream is applied every night for 3 weeks. If necessary the course is repeated after an interval of one week, during which withdrawal bleeding may occur.
2. Acid vaginal douches as dilute acetic acid or lactic acid (1/2-1%) once or twice daily.

In resistant cases, the uterus is curetted to exclude carcinoma of uterus or associated senile endometritis. Antibiotics are not used to treat senile vaginitis.

TRICHOMONAS VAGINITIS

It is the third most common cause of abnormal vaginal discharge in the adult woman (20%) after Candidal vaginitis (30%), and bacterial vaginosis (40-50%).



Fig.49. *Trichomonas vaginalis*

Causative Organism

The *Trichomonas vaginalis* is a flagellated parasite (protozoon). It is ovoid or pear-shaped and slightly larger than a leucocyte. It has 4 anterior flagellae, undulating membrane and a long tail. *T. vaginalis* is different from *Trichomonas* found in the mouth (*T. Buccalis*) and that found in the intestine (*T. hominis*). The optimum pH for trichomonads is 5.5-6.5 i.e. weak acid medium, so symptoms usually start immediately after menstruation as the alkaline menstrual blood reduces vaginal acidity.

Mode of Infection

1. Sexual intercourse. The organism may be found in the prepuce, urethra, prostate or seminal vesicles of the husband. Incubation period 3-30 days.
2. Contamination from infected towels, instruments, lavatory seats, and swimming pools.
3. Infection from the rectum may occur by organisms present in the intestinal tract. This explains infection in virgins.
4. *Trichomonas vaginalis* is present in the vagina in about 2-3% of women without producing symptoms i.e. carrier state. Change in the general or local resistance as in case of severe illness can change the carrier state into an infected state.

Diagnosis

Symptoms

1. Vaginal discharge. It is the main complaint. Typically it is excessive, yellow, offensive and frothy. However, the nature of the discharge varies widely. Frothiness is due to the action of trichomonads on glycogen with production of carbon dioxide gas.
2. Pain and soreness of the vulva secondary to irritation by vaginal discharge.
3. Pruritus vulvae.
4. Dyspareunia due to tenderness of the vagina.
5. Frequency and burning micturition if there is *Trichomonas* cystitis or irritation of urethral meatus.

Signs

1. The vulva may be inflamed, red and tender.
2. The vaginal mucosa is inflamed, red and tender. Red spots may be seen specially on the portio vaginalis of the cervix and in the vaginal fornices. These spots do not bleed on touch and give the mucosa a "strawberry" or "flea-bitten" appearance which is present in less than 25% of cases
3. The cervix may be free, or it may show red spots like the vagina.

Investigations

The diagnosis is confirmed by demonstrating the *Trichomonas vaginalis* by one or more of the following methods:

1. Fresh drop examination (wet smear). A drop of vaginal discharge is put on a slide, add a drop of normal saline warmed to body temperature (to keep the trichomonads motile), cover with a slip and examine at once. Under the low power magnification, the trichomonads are known by their shape, size (slightly larger than a pus cell) and rotatory movements. Many pus cells are usually present. Under high power magnification, one can observe the movement of flagellae and undulating membrane. The wet smear may miss up to 30% of cases.
2. Stained film. In Gram stained smear the trichomonads appear dark red (Gram negative).
3. Culture on specific media (Kupferberg or Feinberg medium). It is the best method for diagnosis.

Treatment

The husband and wife must be treated at the same time, to prevent reinfection of the wife (ping-pong infection). The drug of choice is metronidazole (Flagyl). It is given in the form of oral tablets, one tablet, 250 mg three times daily or one tablet, 500 mg twice daily for seven days for both wife and husband. Metronidazole can be given as 2 grams in a single dose. Metronidazole vaginal tablet (500 mg) can be inserted every night for 7 days. The vaginal tablets are less effective as the organisms may be found in other sites as the bladder or urethra

and Bartholin glands. The indications for local therapy are: (1) nausea and vomiting occurring with oral medication; (2) lactating women as the drug is excreted in milk. At the same time the wife may use an acid vaginal douche as dilute lactic acid every night. Coitus is avoided during treatment. The cure rate of oral metronidazole is about 90%. Failure of therapy may be due to poor intestinal absorption, resistant organisms or reinfection from the untreated husband. In resistant cases we double the dose and duration of therapy to be 14 days. Tinidazole (Fasigyn-500 mg tablet), can be given orally in a single dose of 4 tablets (2 gm) for both wife and husband.

Note. *Trichomonas vaginalis* may lead to premature rupture of membranes, preterm labour, infection after abortion, and caesarean section.

CANDIDA (MONILIAL) VAGINITIS

"VULVOVAGINAL MYCOSIS"

Causative Organism

Infection is caused by a fungus called *Candida* or *Monilia*. There are several species as *Candida albicans*, *C. tropicalis*, and *C. glabrata*. *C. albicans* is responsible for infection in the majority of cases (90%). It is the second most common cause of vaginitis after bacterial vaginosis. It is oestrogen dependent infection, and so it is rare before menarche, and after menopause.

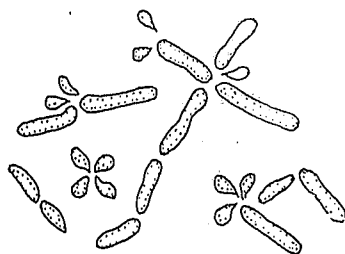


Fig. 50. *Candida albicans*

Predisposing Factors

1. Presence of carbohydrate (glycogen or glucose). This explains why infection is common in pregnant and diabetic women.
2. High vaginal acidity. This destroys other bacteria thus allowing the fungus to flourish. This explains why the symptoms are relieved by douching with 1% sodium bicarbonate solution.
3. Broad spectrum antibiotic therapy destroys other bacteria allowing the fungus to flourish. This is the main cause of recurrent infection.
4. The use of combined contraceptive tablets which increase the amount of glycogen in the vaginal mucosa. Oestrogen also directly stimulates the growth of the fungus. This applies to the high - but not to the low-dose oestrogen pills.
5. Corticosteroid therapy and immunosuppressive drugs.
6. Increased local moisture due to hot, moist weather or tightly fitting clothes.

Mode of Infection

1. *Candida albicans* is present in the vagina of about 25% of women without producing symptoms. However, the carrier state may be changed into the infected state by the above mentioned predisposing factors.

2. Contamination from infected towels, instruments, lavatory seats, and swimming pools.
3. Infection from the rectum may occur by organisms present in the intestinal tract.
4. Sexual intercourse. An infected diabetic husband with monilial urethritis or balanitis may infect his wife. This method of spread is rare.

Diagnosis

Symptoms

1. Vaginal discharge. Typically, it is thick, white, scanty and curdy like cottage cheese, however, the nature of discharge varies widely. It is odourless, though some patients notice the smell of yeast. An offensive discharge occurs when other bacteria are present as well.
2. Pain and soreness of the vulva secondary to irritation by vaginal discharge.
3. Pruritus vulvae. It is the main complaint, usually out of proportion to the amount of discharge.
4. Dyspareunia due to tenderness of the vagina.
5. Frequency and burning micturition due to irritation of urethral meatus.

The symptoms are usually exacerbated during the week before menstruation, due to increased glycogen content of vaginal mucosa. Some relief occurs with the onset of the flow as menstrual blood is alkaline in reaction.

Signs

1. The vulva may be inflamed, red and tender.
2. The vaginal mucosa is inflamed, red and tender. The discharge tends to form white patches which are adherent to the vaginal wall. Removal of these patches may cause slight bleeding.

Investigations

- A. The diagnosis is confirmed by demonstrating the fungus by one or more of the following methods:
 1. Wet smear. A drop of normal (physiologic) saline is added to a drop of discharge on a slide, cover with a slip and examine microscopically. The fungus appears as long thin filaments (mycelia) to which small buds are attached here and there. We can use 10% potassium hydroxide solution instead of normal saline. This alkaline solution breaks up all the cells except *Candida*.
 2. Vaginal pH is normal; 3.5-4.5. A pH more than 4.5 excludes candidiasis.
 3. Stained film. Using Gram, methylene blue, or gentian violet stain. *Candida* is Gram positive and appears violet.
 4. Culture on specific media as Nickerson medium. It is the best method of diagnosis, but rarely needed. The Feinberg medium allows growth of both *Candida* and *Trichomonas vaginalis*.

5. The use of Micro-Stix. The strip changes in colour when dipped into monilial discharge. It is costly.
- B. Urine analysis or fasting blood sugar must be done in every case to exclude diabetes mellitus.

Treatment

1. One of the azole drugs is given:
 - a. Clotrimazole (Canesten) vaginal tablets and cream for itching. One tablet, 100 mg is inserted every night for 6 nights, or a single tablet, 500 mg is inserted once. Cream is applied twice daily.
 - b. Miconazole (Gyno-Daktarin) vaginal ovules and cream. One ovule, 400 mg every night for 3 nights.
 - c. Oral medication. Itraconazole (Sporanox) capsules. Two capsules are given and repeated after 12 hours. Fluconazole (Diflucan), only one capsule (150 mg) is given orally. These drugs are contraindicated during pregnancy and lactation.
2. Alkaline vaginal douches as 1% sodium bicarbonate solution.
3. Management of predisposing factors as control of diabetes and temporary stopping of contraceptive tablets.
4. Vitamin B complex oral tablets to inhibit the growth of monilia.
5. Boiling of the underclothes which should be of cotton (avoid nylon underwear). Wiping the anus front to back.

Notes

- Candida vaginitis is frequent during pregnancy because:
 1. Vagina is rich in glycogen;
 2. High vaginal acidity;
 3. Renal glycosuria is frequent;
 4. Low immunity due to decreased T-cell activity.

In fact it is present in more than 20% of pregnant women.
- The use of gentian violet solution is outmoded because it is messy and can cause severe local allergic reaction with exfoliation of the epithelium.

Note for the postgraduate

Recurrent vulvo-vaginal mycosis is defined as 4 or more attacks of candidiasis per year. Antibiotic therapy is the main cause of recurrent infection. Other causes include diabetes, pregnancy, high-dose combined contraceptive tablets, corticosteroid therapy, immunosuppressive therapy, re-infection from intestinal tract, re-infection from the husband, and infection with non-albicans species as *C. tropicalis* and *C. glabrata* which need longer treatment with azole drugs. In a patient with recurrent infection culture of vaginal discharge is necessary for 2 reasons: (a) a non-albicans organism may be responsible for the infection; (b) in about 50% of cases, the discharge is not due to yeast infection, but due to human papillomavirus infection which is detected by biopsy of the vaginal introitus. Treatment of recurrent infection is by treating any predisposing factor as control of diabetes, and giving a long course of an oral azole drug in a reduced dose as fluconazole (Diflucan) 50 mg once weekly for 3 to 6 months; Alternatively, a weekly vaginal tablet may be used; 100, 200 or 500 mg, depending on which dose controls the symptoms.

BACTERIAL VAGINOSIS (B.V.)

It is the most common cause of abnormal vaginal discharge in the adult woman (40-50%). Infection is caused by a group of anaerobic organisms which include *Gardenerella* (*G*) *vaginalis*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, *Peptostreptococci*, *Mobiluncus* species, *Bacteroides*, and other organisms. *G. vaginalis* is present in most cases (70-90%) but not necessarily in every case. It is a Gram-variable coccobacillus. The organisms replace the Döderlein bacilli which are absent or few.

Mode of Infection

It is not known, however, the following are predisposing factors:

1. Sexual intercourse. Coitus starting at an early age, and multiple sexual partners. It is suggested that with increased frequency of intercourse, the alkaline semen reduces the vaginal acidity allowing growth of anaerobic bacteria. It is not a sexually transmitted disease as no organism is transmitted from the husband.
2. Excessive use of alkaline vaginal douches. Also douches may aid the bacteria to reach the upper genital tract.
3. Washing the vulva with soap (alkaline medium).
4. The use of intrauterine device. The tail of the device may favour the growth of anaerobic bacteria.
5. A phage virus infects the lactobacilli and decreases their number allowing growth of anaerobic micro-organisms.
6. Autoinfection from intestinal flora.
7. Black women, lesbianism, and smoking.

Symptoms

The condition is asymptomatic in up to 50% of cases. The only symptom is vaginal discharge which is white or gray in colour, excessive, thin, and offensive with a fishy odour. The smell may be only noticed during intercourse. The classic discharge looks like a cup of milk which has been poured into the vagina. The offensive odour is due to the formation of amines from amino acids by enzymes (decarboxylases) produced by the anaerobic bacteria and so the condition is sometimes called anaerobic vaginosis. There is no dyspareunia, vulval soreness or pruritus as there is no inflammatory reaction, hence the term vaginosis and not vaginitis (pus cells are absent or rare).

Diagnosis

Three out of 4 signs should be present for the diagnosis:

1. White or gray, excessive, thin, and offensive vaginal discharge with a fishy odour.
2. Vaginal pH more than 4.5 (a pH below 4.5 excludes B.V.). Normal vaginal pH is 3.5-4.5.
3. A positive whiff (sniff or amine) test.

4. The presence of clue cells which must form more than 20% of the exfoliated vaginal epithelial cells. They are detected by a saline wet smear or Gram stained film.

The amine (whiff) test is performed by adding a drop of 10% potassium hydroxide (alkaline solution) to a drop of vaginal discharge on a slide. Amines (as cadavarine) are released giving a fishy odour. Clue cells are exfoliated vaginal epithelial cells covered with large numbers of bacteria, so the cell borders become obscured. They appear under the microscope after adding a drop of normal saline to a drop of the vaginal discharge (wet smear). They can also be detected by a Gram stained film. They are called "clue cells" because their presence gives a clue to the diagnosis. Culture has no role in the diagnosis of bacterial vaginosis.

New methods of diagnosis include measuring the metabolic products of anaerobic bacteria such as aminopeptidase, and the use of DNA probes which detect the antigen of *C. vaginalis*.

Complications

Bacterial vaginosis in pregnancy can lead to abortion in the second trimester, chorioamnionitis, premature rupture of membranes, preterm labour, postabortive infection, and postpartum endometritis. In the nonpregnant patient it causes pelvic inflammatory disease, urinary tract infection, and pelvic infection (parametritis) after hysterectomy.

Treatment

B.V. is treated with metronidazole (Flagyl), or clindamycin. Metronidazole is the drug of choice and is given as in *Trichomonas vaginitis*. It is given in the form of oral tablets; one tablet 250 mg three times daily or one tablet 500 mg twice daily for 7 days. It can be given as 2 grams in a single dose. Metronidazole vaginal tablet (500 mg) can be inserted every night for 7 days. Also metronidazole gel (Metrogel) can be used locally. Oral clindamycin 300 mg twice daily for 7 days or local clindamycin in the form of a vaginal cream applied once daily for 7 days. Also clindamycin vaginal ovule once daily for 3 days. During pregnancy we can give metronidazole or clindamycin. The husband is not treated as this does not increase the cure rate or prevent recurrence of infection. The responsible organisms are not sexually transmitted.

Notes

1. Offensive vaginal discharge is caused by *Trichomonas vaginitis*, Bacterial vaginosis, the presence of semen in the vagina, and foreign body.
2. The small dose of local therapy with metronidazole reduces the systemic side effects.

Notes for the postgraduate

1. Döderlein bacilli increase vaginal acidity which kills the pathogenic bacteria. Also some of its species produce hydrogen peroxide which is toxic for many anaerobes.
2. The combined contraceptive tablets protect against B.V. Oestrogen increases the amount of glycogen in the vaginal mucosa and raises vaginal acidity.
3. Some anaerobes produce succinate which inhibits the killing power of leucocytes. This may explain why B.V. does not produce inflammatory reaction and pus cells are absent or rare, hence the name vaginosis and not vaginitis.

4. The Whiff test can be positive in *Trichomonas* vaginitis.
5. The condom protects against B.V., possibly the alkaline semen will not reduce the vaginal acidity.

NONSPECIFIC VAGINITIS

It is vaginal inflammation in absence of a specific organism as the gonococcus or *Trichomonas*. Vaginitis is due to organisms as streptococci, staphylococci, and *E. coli*. This can occur before puberty or after menopause as the vaginal acidity is low and the vaginal epithelium is thin and can be infected by nonspecific bacteria. However, in the adult woman the vaginal epithelium is thick and can resist these nonspecific bacteria and every effort should be done to find a specific cause for vaginitis. Nonspecific vaginitis of children and postmenopausal patients is best treated with local oestrogen.

VAGINITIS EMPHYSEMATOSA

It is a rare condition, mostly seen in pregnant women. There are numerous small bullae in the vaginal epithelium which are filled with carbon dioxide gas. The surrounding tissues are hard and indurated and there is excessive purulent discharge. The true cause is unknown, but may be due to *Trichomonas* or *Gardenerella vaginalis*. Treated with metronidazole.

CYTOLYTIC VAGINITIS

Causative Organism

Overproduction of Döderlein bacilli is responsible for the condition. Some species of these bacilli produce hydrogen peroxide. Increased production of the latter causes vaginal irritation and cytolysis of vaginal cells.

Diagnosis

Symptoms

1. Vaginal discharge which is white or paste-like.
2. Pain and soreness of the vulva secondary to irritation by vaginal discharge.
3. Pruritus vulvae.
4. Dyspareunia.
5. Frequency and burning micturition.

Investigations

1. Wet smear. It shows increased number of Döderlein bacilli and the vaginal cells show cytolysis. Specific organisms as *Trichomonas*, *Candida*, and *Gardenerella vaginalis* are absent.
2. Vaginal pH is less than 4.5.

Treatment

Alkaline vaginal douches using sodium bicarbonate (30-60 g/litre) 2 or 3 times per week and continued till symptoms disappear.



CERVICITIS

Inflammation of the endocervix may be acute or chronic.

ACUTE CERVICITIS

Aetiology

(1) Gonorrhoea; (2) chlamydial infection; (3) puerperal infection after abortion or labour; (4) cauterization of cervix; (5) postoperative, e.g., after dilatation of the cervix.

Symptoms

(1) Mucopurulent vaginal discharge; (2) pelvic pain and low backache; (3) dyspareunia.

Signs

The cervix is swollen and deep red in colour (angry looking cervix). A mucopurulent discharge exudes from the external os. Marked tenderness occurs if the cervix is moved from side-to-side.

Treatment

Antibiotics are given. Any local treatment is contraindicated to prevent ascent of infection.

Note. If acute cervicitis is not properly treated it tends to become chronic because: (1) the endocervical mucosa is thrown into rugae and this interferes with drainage of infection; (2) the cervical mucosa does not shed during menstruation.

CHRONIC CERVICITIS

It is a common gynaecological lesion. It is the result of acute cervicitis or it is due to a mild infection from the start.

Causative Organisms

Gonococci, Chlamydia trachomatis, and nonspecific organisms as streptococci, staphylococci, and Escherichia coli. Tuberculosis, bilharziasis, and syphilis are rare causes of chronic cervicitis.

Diagnosis

Symptoms

The condition may be asymptomatic. However, the patient may complain of one or more of the following:

1. Vaginal discharge. It is mucoid or mucopurulent, and sometimes blood stained; (the mucus is due to overactivity of the secretory cells of the cervical canal).
2. Contact bleeding is liable to occur with vascular erosion or mucous polypi (bleeding during intercourse, vaginal examination or douching).
3. Soreness and pruritus vulvae due to irritation of vulva by discharge.
4. Low backache (sacralgia), due to spread of infection along the uterosacral ligaments.

5. Pain in the lower abdomen or iliac fossa, due to spread of infection causing chronic parametritis.
6. Dyspareunia if infection has caused parametritis. Pain is produced when the cervix is moved laterally.
7. Symptoms of pelvic congestion as congestive dysmenorrhoea and menorrhagia.
8. Infertility. Cervicitis destroys the secretory cells of the endocervix making the cervical mucus scanty and thick preventing the ascent of spermatozoa. Also pus cells affect sperm motility and migration.
9. Frequency and burning micturition. Infection may spread to the bladder by lymphatics causing cystitis.
10. Rheumatic pains and allergic manifestations because chronic cervicitis acts as a septic focus.

Signs

The cervix will show one or more of the following lesions:

1. **Chronic endocervicitis.** The cervix looks more or less normal, but there is a mucopurulent discharge escaping from the external os because infection is limited to the mucous membrane of the cervical canal.
2. **Cervical erosion (ectopy).** This appears as a bright red area around the external os.
3. **Mucous polypi of the cervix.** These appear as one or more soft, bright or dark red swellings projecting from the external os. The polyp has a pedicle arising from the endocervix. Infection causes hyperplasia of the endocervical epithelium and polyp formation. The polyp may bleed on touch.
4. **Chronic hypertrophic cervicitis.** The cervix is enlarged, congested and firm in consistency due to excessive fibrosis. It is due to long-standing infection of the cervix or chronic congestion as in case of prolapse.
5. **Ectropion.** If the cervix is bilaterally torn, the anterior and posterior lips become everted, thus exposing the endocervix.
6. **Nabothian follicles or cysts.** The openings of cervical glands (crypts) become obstructed by plugs of mucus, pus, epithelial cells or fibrosis. The glands become distended with secretion forming follicles or cysts. They appear blue if they contain mucus, or yellow if they contain pus.

Note. Bilateral cervical tears cut the circular muscle fibres, and contraction of the longitudinal fibres leads to ectropion.

Investigations

1. Bacteriological study of the cervical discharge by culture to exclude specific organisms as gonococci and Chlamydia.
2. Cervical smear or colposcopic examination to exclude malignancy.

Complications

(1) Ascending infection as salpingitis. This is liable to occur after abortion, labour or hysterosalpingography; (2) cystitis due to spread of infection by lymphatics; (3) infertility; (4) rheumatic pains and allergic manifestations due to the presence of a septic focus.

Note. Chronic cervicitis, cervical erosion and lacerations are no longer considered aetiological factors in cervical carcinoma.

Differential Diagnosis of Cervical Erosion

See differential diagnosis of ulcerative lesions of the cervix mentioned with cervical carcinoma.

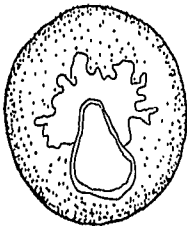


Fig. 51. Mucous polyp of the cervix

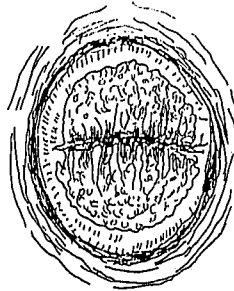


Fig. 52. Cervical erosion

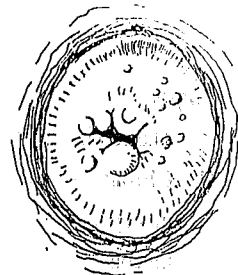


Fig. 53. Nabothian follicles

Treatment of Chronic Cervicitis

1. Medical Treatment

Vaginal douches and insertion of antiseptic vaginal tablets as Albothyl every night. This treatment gives temporary relief, it is not curative because infection is deep seated in the cervical canal and cannot be reached by drugs applied locally. Except in case of gonorrhoea and chlamydial infection, systemic antibiotics are useless because an active infection is not present.

2. Cauterization

The best treatment for nonspecific chronic cervicitis. It may be electric cautery, diathermy cautery, cryocautery, laser cautery, or cold coagulation. Cauterization destroys infected tissues, and surrounding healthy tissues grow to cover the raw area.

Technique of Electric or Diathermy Cauterization

It is done few days after menstruation to give a chance for healing to occur before the next period. It is done without anaesthesia because the cervix is not sensitive to heat but sensitive only to dilatation. However, in a nullipara it is preferable to dilate the cervix up to 5 mm (No. 5 Hegar dilator) under general anaesthesia before cauterization. The electrode is used to cauterize the anterior wall of the cervical canal extending from just below the internal os

downwards to the external os. The posterior wall is then cauterized. The lateral walls are not cauterized to avoid the cervical branch of the uterine artery. The whole area of erosion on the portio vaginalis is also cauterized. Nabothian follicles are punctured and their lining destroyed by cautery. No douching and no sexual intercourse for 2-3 weeks.

Complications of Cauterization

(1) Ascending infection as salpingitis and parametritis; (2) secondary haemorrhage may occur 7-10 days after cautery due to separation of the necrotic tissue; (3) vaginal discharge which gradually disappears within 6 weeks, when the cauterized area becomes covered with stratified squamous epithelium; (4) fibrosis and cervical stenosis and this may lead to dysmenorrhoea, haematometra, infertility or cervical dystocia during labour. Avoided by proper technique and passing a uterine sound after healing is complete.

Cryocautery

Cautery by deep freeze may be used, it allows better healing and complications as haemorrhage, infection and fibrosis are less. However, it causes a profuse vaginal discharge for 2-3 weeks postoperatively. Carbon dioxide, nitrous oxide or nitrogen – all in liquid state – are passed through a hollow probe placed in the cervical canal and against the external os. Freezing (-60°C) is allowed for 2-4 minutes but not more.

Laser Cautery

Laser beam is used to destroy infected tissues. Complications as haemorrhage, infection and fibrosis are less and with rapid healing. However, it is costly and needs experience.

Cold Coagulation

Using Semm cold coagulator. The technique destroys tissues by heat. However, the temperature reaches only 100°C . Cold coagulation is a misnomer as it is cold relative to the high temperature of electrocautery.

Note. A cervical smear is taken or the cervix is examined by the colposcope before cautery to exclude malignancy.

3. Surgical Treatment

- a. Trachelorrhaphy. Infected cervical lacerations are excised and the cervix is reconstructed by a plastic operation.
- b. Conization. Performed when the endocervix and portio vaginalis are much affected by laceration and infection.

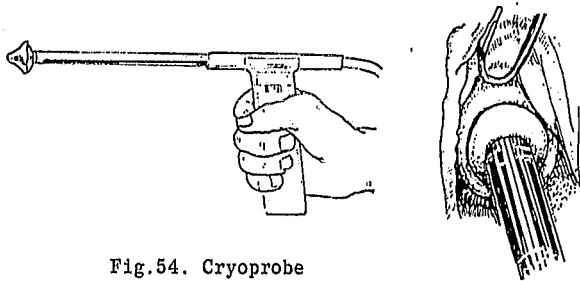


Fig.54. Cryoprobe

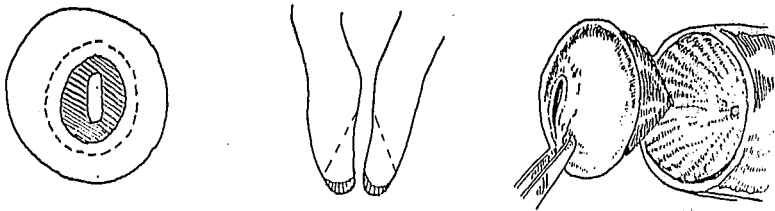


Fig.55. Conization of the cervix

CERVICAL EROSION (ECTOPY)

Definition

It is an area around the external os of the cervix covered by columnar epithelium instead of the squamous epithelium which normally covers the portio vaginalis. It is bright red in colour because the columnar epithelium is thin and shows the colour of the blood in the underlying blood vessels.

Aetiology

1. **Congenital erosion.** Due to persistence of the condition found during the intrauterine life where the columnar epithelium of the cervical canal covers a variable area of the portio vaginalis around the external os. Normally, at full term, the portio vaginalis of the cervix becomes completely covered by squamous epithelium except in about one-third of cases when it remains covered by columnar epithelium giving rise to a congenital erosion.
2. **Hormonal erosion.** This is caused by a relative excess of oestrogen. This hormonal imbalance stimulates the columnar epithelium to grow at the expense of the squamous epithelium. This explains why erosion is frequent during pregnancy and in patients taking contraceptive tablets (pill ectopy). The lesion disappears 3-6 months after delivery.

Note. Chronic cervicitis is no more considered a cause of cervical erosion.

Clinical Types of Erosion

1. **Simple or flat erosion.** The columnar epithelium forms a flat layer around the external os.
2. **Papillary erosion.** The columnar epithelium grows in the form of papillae which are raised on the surface. The surface of the erosion becomes irregular and gives a velvety feeling on touch.

3. **Follicular or cystic erosion.** The openings of the cervical glands become obstructed by plugs of mucus, pus, epithelial cells or fibrosis. The glands become distended with secretion forming nabothian follicles or cysts which appear under the columnar epithelium of an erosion. They appear blue if they contain mucus, or yellow if they contain pus.

Symptoms

The condition may be asymptomatic, however, the patient may complain of:

1. Vaginal discharge. It is mucoid due to increased secretory area. It becomes mucopurulent if secondary infection occurs. Sometimes it is blood stained when the tissues are congested.
2. Contact bleeding.
3. If secondary infection occurs, as the columnar epithelium has low power of resistance, symptoms of chronic cervicitis may occur in the form of soreness and pruritus vulvae, low backache, pain in the lower abdomen or iliac fossa, dyspareunia, symptoms of pelvic congestion as congestive dysmenorrhoea and menorrhagia, infertility, frequency and burning micturition, rheumatic pains and allergic manifestations.

Signs

1. A papillary erosion gives a velvety feeling on touch.
2. A vascular erosion gives contact bleeding on touch.
3. Speculum examination shows a bright red area around the external os.



Investigations

Cervical smear or colposcopic examination to exclude malignancy.

Treatment

Asymptomatic erosion does not require treatment. When symptoms are present treatment is by cauterization (see before).

Note. Postpartum erosion is left for 3 months as spontaneous cure may occur. Congenital or nulliparous erosion is usually not infected and requires no treatment.

PYOMETRA

It is a collection of pus within the uterus.

Aetiology

(1) Endocervical carcinoma; (2) endometrial carcinoma; (3) senile endometritis; (4) tuberculous endometritis; (5) puerperal endometritis and septic abortion; (6) congenital atresia of cervix or vagina; (7) stenosis of cervix or vagina following operations or radiotherapy; (8) infected submucous fibroid; (9) intrauterine contraceptive device.

Clinical Picture

A. Symptoms:

1. General symptoms of infection as fever and rigors.
2. Suprapubic pain.
3. Intermittent purulent vaginal discharge.

B. Signs:

1. Patient is feverish and toxic.
2. The uterus is symmetrically enlarged, soft, and tender.
3. The passage of a uterine sound is followed by a discharge of pus.

Investigations

Pus is sent for aerobic and anaerobic culture and sensitivity test.

Treatment

1. Drainage. Under general anaesthesia the cervix is dilated and a rubber tube is fixed for drainage.
2. Ergot preparations to help drainage by contracting the uterus.
3. Antibiotics, according to culture and sensitivity test.
4. Uterine curettage is done one week after drainage to exclude a malignant tumour.
5. Hysterectomy for resistant cases.

PELVIC INFLAMMATORY DISEASE (PID)

It means infection of the upper genital tract i.e. infection of the uterus, fallopian tubes, ovaries, as well as the parametrium, and pelvic peritoneum. When the term is used it does not indicate the actual site of infection but simply indicates infection affecting any part of the upper genital tract. However, if the site of infection could be determined by laparoscopy, laparotomy or endometrial biopsy then the anatomical site of infection is mentioned as endometritis, salpingitis, etc. Frequently, PID is used to describe salpingo-oophoritis.

SALPINGITIS AND SALPINGO-OOPHORITIS

Infection of the tube is usually bilateral and usually associated with involvement of the ovaries. Infection may be acute or chronic.

AETIOLOGY

A. Causative Organisms

1. *Chlamydia trachomatis* (40-50%). It is the most common responsible organism in Sweden, the United States and many European countries.
2. Gonococci. Responsible for about 25% of cases.

3. Streptococci and staphylococci. Following abortion or labour.
4. *Escherichia (E.) coli* from adherent bowel as in case of appendicitis, and diverticulitis.
5. *Mycoplasma* species (*M. hominis*, *M. genitalium*, and *Ureaplasma urealyticum*).
6. Anaerobic organisms e.g. *bacteroides*, *peptococci*, and *Clostridium* species.
7. Tubercle bacilli.
8. *Schistosoma haematobium*.
9. Actinomycetes. These may cause infection in the presence of intrauterine contraceptive device.
10. Other organisms as pneumococci and typhoid bacilli.

B. Routes of Infection

1. Ascending infection. It is the commonest method (99%). In gonococcal and chlamydial infection the organisms pass upwards along the lumen of uterus and tubes. In cases of abortion or labour the streptococci and staphylococci pass along the parametrial lymphatics and veins. Ascending infection may occur after hysterosalpingography, dilatation and curettage or due to the presence of an intrauterine contraceptive device.
2. Spread from an adherent infected organ as in case of appendicitis or diverticulitis.
3. Bloodborne infection as in case of tuberculosis, bilharziasis and tonsillitis.

Note. Acute infection is by a single organism mostly Chlamydia. Chronic infection is polymicrobial.

ACUTE SALPINGITIS

Pathology

1. **Acute catarrhal salpingitis.** Infection is mild and resistance of the patient is high. Infection is limited to the mucous membrane which becomes congested, red and oedematous. The lumen contains a serous exudate. It usually undergoes complete resolution or forms a hydrosalpinx.
2. **Acute suppurative salpingitis.** Infection is severe and involves all the layers of the tube which become infiltrated with polymorphs. The lumen contains a purulent exudate. It may lead to the formation of a pyosalpinx. Gangrenous infection never occurs because the tube has a double blood supply (uterine and ovarian arteries).
3. **Acute perisalpingitis.** It may occur after abortion or labour when the organisms as streptococci and staphylococci spread along the parametrial lymphatics and veins to attack the tube from outside. It also follows spread of infection from the surrounding viscera as the appendix. Excessive peritubal adhesions form, and the fimbrial end may be closed.

Diagnosis

1. History

There may be a history of recent abortion, labour, gonococcal infection or operation as curettage or hysterosalpingography. In most cases symptoms appear during menstruation, or shortly after the cessation of menses due to absence of antibacterial action of cervical mucus.

2. Symptoms

- a. Sudden onset of severe lower abdominal pain bilateral in nature, but occasionally unilateral (5%).
- b. Mucopurulent vaginal discharge if there is associated cervicitis.
- c. A menstrual period may occur early due to pelvic congestion and is usually severe.
- d. Dysuria and frequency of micturition.
- e. General symptoms of infection in the form of fever, rigors, and nausea with or without vomiting.

3. Signs

General Examination

There is fever (38°C and above) and rapid pulse.

Abdominal Examination

Lower abdominal tenderness and rigidity. Maximal tenderness is at the tubal points (half an inch above the middle of the inguinal ligament).

Vaginal Examination

It should begin with speculum examination to take 3 swabs; one from the cervical canal to detect Chlamydia, another one from the cervical canal to detect Gonococci, the third one from the posterior vaginal fornix for aerobic and anaerobic bacteria. The specimens are examined by microscopy, and culture and sensitivity test. On bimanual examination the lateral vaginal fornices are very tender and pain is produced when the cervix is moved from side-to-side (this puts tension on the broad ligament and affected tube causing pain). This is called "Chandelier sign". It is often difficult to feel the uterus and adnexa because of tenderness and rigidity.

4. Investigations

(a) Examination of cervical and vaginal swabs as mentioned above; (b) blood picture shows leucocytosis in 50% of cases; (c) sedimentation rate may be raised (in 75%); (d) C-reactive protein may be raised (in 80%); (e) urine analysis to exclude cystitis and pyelonephritis; (f) sonography to diagnose adnexal or pelvic mass; (g) laparoscopy is done if the cause of pain is not clear. It is the most accurate way to diagnose salpingitis. It is also done if the patient is not responding to treatment. Also done in case of recurrent pelvic pain.

Differential Diagnosis

(1) Causes of acute abdominal pain as acute appendicitis and disturbed ectopic pregnancy, etc. (2) acute parametritis; (3) cystitis and pyelonephritis.

Treatment

1. Admission to hospital is indicated in all cases with acute PID. However, women with mild symptoms may be treated as outpatients.

2. Complete rest in bed in semisitting position to limit infection to the pelvis.
3. Light diet and excessive fluids.
4. Antibiotics. A combination of drugs is given to act against Gonococci, Chlamydia, aerobic and anaerobic bacteria e.g. gentamycin and clindamycin are given intravenously for at least 4 days followed by oral clindamycin for 10-14 days. For outpatient therapy we can give ciprofloxacin 500 mg orally twice daily plus metronidazole 500 mg orally twice daily for 14 days. Ciprofloxacin acts against both Chlamydia and Gonococci.
5. Relief of pain by application of heat to the lower abdomen by a thermopad. Analgesics are given if diagnosis is definite.
6. Surgical treatment is indicated in the following conditions: (a) formation of a pelvic abscess. In this case the posterior vaginal fornix is incised (posterior colpotomy) and drainage is maintained by inserting a rubber tube; (b) formation of ovarian abscess; (c) rupture of a pyosalpinx; (d) spreading of peritonitis in spite of treatment.

Note for the postgraduate

The diagnostic laparoscopic criteria of acute salpingitis include erythema and/or oedema of the fallopian tube, exudate from the fimbrial end, fluid in Douglas pouch, fimbrial agglutination, pyogenic membrane on the serosa, and presence of inflammatory masses. The exudate from the fimbrial end and fluid in Douglas pouch contain white blood cells and bacteria. Specimens are taken for culture and sensitivity.

CHRONIC SALPINGITIS

It is always preceded by acute or subacute salpingitis except in certain conditions as tuberculosis and bilharziasis when infection is chronic from the start.

Pathology

1. **Hydrosalpinx.** It is the result of catarrhal salpingitis. The fimbrial end of the tube is closed by adhesions and the tube becomes distended with clear serous fluid forming a retort-shaped swelling. The interstitial part of the tube remains patent, hence hydrosalpinx can be diagnosed by hysterosalpingography. It rarely exceeds the size of an orange. Peritubal adhesions are absent or minimal so a hydrosalpinx can undergo torsion. In some cases the fluid of a hydrosalpinx escapes from its uterine end leading to intermittent escape of serous discharge from the vagina. This condition is known as intermittent hydrosalpinx (hydrops tubae profluens). The discharge of fluid into the uterine cavity may prevent implantation of the embryo after In Vitro Fertilization (in 50%), and it is recommended to perform salpingectomy before the procedure to improve the results.

Complications. (a) Torsion and haematosalpinx; (b) secondary infection from the bowel and formation of pyosalpinx; (c) rupture due to trauma, e.g. bimanual examination.

2. **Pyosalpinx.** It is the result of suppurative salpingitis or secondary infection of a hydrosalpinx. It is retort-shaped. The tubal wall is thick fibrous and infiltrated with inflammatory cells. The tube is surrounded by dense adhesions and so the uterus may

become fixed in retroversion. Because the wall is thick, a pyosalpinx does not reach a large size.

Complications. (a) Rupture and peritonitis; (b) tubal fistula, a pyosalpinx may open into the bladder, vagina, or intestine; (c) recurrent attacks of acute salpingitis; (d) chronic ill-health and rheumatic pains because it acts as a septic focus.

3. **Chronic interstitial salpingitis.** Infection affects mainly the muscle layer. The wall of the tube is thick, fibrous and may show interstitial abscesses. The lumen becomes stenosed and this predisposes to tubal pregnancy.
4. **Salpingitis isthmica nodosa.** The wall of the tube shows nodules, 1-2 cm in diameter particularly in the region of the isthmus. The lesion is bilateral in 80% of cases. Microscopically the nodule consists of hypertrophied muscle containing gland spaces lined by tubal epithelium. The true cause is unknown but most probably it is a postinflammatory lesion occurring with gonococcal, tuberculous, bilharzial, and nonspecific salpingitis. Sometimes it is considered to be due to congenital malformation. Endometriosis of the tube may cause nodular swellings but the gland spaces are lined by endometrial tissue.
5. **Tubo-ovarian cyst.** A hydrosalpinx communicating with a follicular cyst of the ovary.
6. **Tubo-ovarian abscess.** A pyosalpinx communicating with an ovarian abscess.
7. **Perisalpingitis.** Active infection disappears leaving the tube surrounded by adhesions. These adhesions may cause kinking of the tube, fixed retroversion or chronic intestinal obstruction.
8. **Chronic specific salpingitis** due to tuberculosis, bilharziasis or actinomycosis.

Notes

1. A hydrosalpinx or pyosalpinx is retort-shaped because the muscle layer in the wall of the ampulla is thin and distends easily, while the muscle layer in the isthmus is thick and resists dilatation.
2. Culture of pus from a pyosalpinx does not show gonococci but other organisms as *E. coli*. See chronic gonorrhoea.

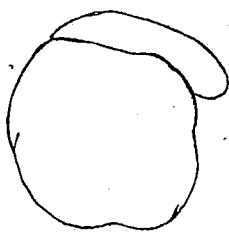


Fig. 56. Hydrosalpinx

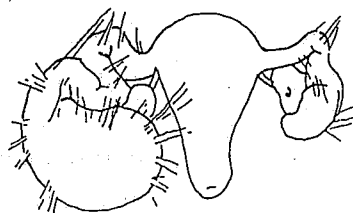


Fig. 57. Bilateral pyosalpinx

Diagnosis

Symptoms

The patient may complain of one or more of the following:

1. A continuous dull aching lower abdominal pain and backache.

2. Symptoms of pelvic congestion in the form of congestive dysmenorrhoea, menorrhagia, polymenorrhoea and increased normal vaginal discharge (leucorrhoea).
3. Dyspareunia due to the presence of inflamed tender swellings in Douglas pouch.
4. Dysuria and dyschezia if extensive adhesions have formed in the pelvis. Dysmenorrhoea, dyspareunia, dysuria, and dyschezia form the dys-syndrome.
5. Infertility, as a result of tubal obstruction. It is sometimes the only complaint.
6. General ill-health and rheumatic pains due to the presence of a septic focus.
7. Recurrent attacks of acute salpingitis.

Signs

General Examination

In case of pyosalpinx, the patient may look ill and anaemic.

Abdominal Examination

Tenderness may be detected over the lower abdomen.

Vaginal Examination

In case of hydrosalpinx and pyosalpinx an elongated cystic swelling is felt in the region of the adnexa. It is usually tender and bilateral. The uterus may be fixed in retroversion. In chronic interstitial salpingitis the tubes are thickened and tender. In extensive cases the whole pelvis is filled with a tender indurated mass from which the pelvic organs cannot be differentiated (frozen pelvis). Sometimes pelvic examination does not show any abnormality as in case of perisalpingitis with peritubal adhesions.

Investigations

(1) Complete blood count. It shows leucocytosis if there is a superimposed active infection; (2) sonography to diagnose adnexal or pelvic mass; (3) computed tomography or magnetic resonance imaging to diagnose small masses; (4) laparoscopy as a diagnostic aid in case of chronic pelvic pain.

Differential Diagnosis

(1) Pelvic endometriosis; (2) tuberculosis of pelvic organs; (3) uterine fibromyomata; (4) ovarian and broad ligament tumours; (5) chronic appendicitis; (6) diverticulitis.

Complications

(1) Infertility; (2) increased risk of ectopic pregnancy; (3) chronic pelvic pain.

Treatment

A. Medical Treatment

It should be tried at first in all cases:

1. Local heat in the form of short-wave therapy to the pelvis applied 3 times weekly for at least 24 sittings, and warm vaginal douches every night. Pelvic heat reduces pain and assists resolution of inflammatory reaction.



2. Icthyol in glycerine vaginal pessaries (glycerine is hygroscopic and withdraws fluid to decongest the pelvis while ichthyol is soothing for pain).
3. Treatment of associated cervicitis which is a focus of reinfection of the tube.
4. Analgesics for pain. Nonsteroidal anti-inflammatory drugs as indomethacin (Indocid) can be given.
5. Antibiotics are used only during the acute exacerbation (useless in the chronic stage).

B. Surgical Treatment

Indications

1. Failure of medical treatment to relieve symptoms as pelvic pain.
2. Recurrent attacks of acute salpingitis.
3. Large tubal swelling.
4. Infertility.

Types of Operations

1. Salpingectomy. Removal of the affected tube with or without the corresponding ovary.
2. Hysterectomy and bilateral salpingo-oophorectomy is the treatment of choice in women above the age of 40 if both tubes and ovaries are affected.
3. In case of infertility the aim of operation is to restore tubal patency by salpingolysis (adhesiolysis) to free the tubes from adhesions, salpingostomy (to make an artificial opening in the closed fimbrial end), resection and end-to-end anastomosis, and tubouterine anastomosis. However, in proximal tubal obstruction, transcervical balloon dilatation should be tried at first. In Vitro Fertilization and Embryo Transfer is indicated when tubal obstruction cannot be corrected by surgery and when surgery fails.

Notes for the postgraduate

- The pregnancy rate after tuboplasty ranges between 10-80%. This depends upon the degree of tubal damage. It is about 20% after surgery for hydrosalpinx and 80% after reversal of clip sterilization as the tube is healthy and a small part has been damaged.
- Oophoritis may occur without salpingitis as in case of mumps, influenza and other viruses. It is equivalent to orchitis in the male. Chronic oophoritis may develop as a part of autoimmune disease and lead to premature ovarian failure.

PARAMETRITIS

It is inflammation of the parametrium which is the connective tissue found between the two layers of the broad ligament. It may be acute or chronic.

ACUTE PARAMETRITIS

Aetiology

Infection may spread to the parametrium directly or by lymphatics as a result of: (1) cervicitis; (2) endometritis occurring after abortion or labour; (3) salpingo-oophoritis;

- (4) operation as dilatation and curettage, lower segment caesarean section and hysterectomy; (5) infected malignant tumour in the cervix, endometrium, bladder or rectum; (6) radiotherapy for carcinoma of cervix or endometrium.

Pathology

An inflammatory exudate collects and coagulates between the two layers of the broad ligament to form a stony hard mass surrounding the uterus. The result of parametritis is complete resolution, healing by fibrosis and chronic parametritis or suppuration and abscess formation. The abscess may pass along the round ligament to point at the external abdominal ring, through the greater sacrosciatic notch to appear in the buttock, through the obturator foramen to reach the front of the thigh, along the ureter to reach the perirenal region, or along the obliterated umbilical artery and urachus to reach the abdominal wall and umbilicus. The abscess may open into the bladder, vagina, rectum or peritoneal cavity. The abscess usually points 6-8 weeks after infection. One complication is thrombophlebitis of the veins in the broad ligament, and this may result in septicaemia or thromboembolism.

Clinical Picture

Symptoms appear 7-14 days after infection. There is fever, rapid pulse, lower abdominal pain and backache. Other symptoms include dysuria, diarrhoea and dyschezia. On bimanual examination there is a hard tender mass to one side of the uterus and reaching the lateral pelvic wall. If the swelling is unilateral it pushes the uterus to the opposite side. If abscess forms fluctuation can be detected. Muscular rigidity is absent because the lesion is extraperitoneal.

Treatment

Rest in bed. Antibiotics (a combination of drugs is given as mentioned with acute salpingitis). Heat is applied to the lower abdomen by a thermopad. Heat reduces pain and helps resolution of the inflammatory exudate. If an abscess forms it is opened and drained where it points.

THE TOXIC SHOCK SYNDROME

AETIOLOGY

The syndrome is caused by the staphylococcus aureus which multiplies in the vagina of women who are using tampons for menstrual protection. The organism introduced into the vagina on the inserting fingers, will multiply in the retained menstrual blood and produces an exotoxin which is absorbed through the vaginal wall into the circulation. The toxin (lipopolysaccharide) may also reach the peritoneal cavity by retrograde menstruation to be absorbed rapidly from the peritoneal cavity. The incidence is about 1 in 20,000 menstruating females per year. About 10% of pregnant women harbour Staph. aureus in the vagina, and so

the syndrome can occur in postpartum period. Very rarely the syndrome occurs with the use of vaginal diaphragms, sponges and cervical caps.

CLINICAL FEATURES

Fever, headaches, nausea, vomiting, watery diarrhoea, hypotension, muscle ache, skin erythema and subcutaneous oedema. Confusion and death may occur (3-6%). There is affection of the liver, kidneys, myocardium, thrombocytopenia and sometimes disseminated intravascular coagulation. Symptoms start between the second and fourth day of menstruation.

TREATMENT

Prophylaxis

General hygiene with care in handling and inserting menstrual tampons. Reduce collection of blood in the vagina by changing the tampons 3-4 times by day and using an external pad at night.

Active Treatment

Remove the tampon, take cultures from it and from the upper vagina as well as blood culture. Antistaphylococcal antibiotic is given. Resuscitation and treatment of shock, this is best carried out in an intensive care unit because there is multisystem failure. After recovery, further cultures are taken from the vagina to exclude a carrier state as the syndrome is liable to recur (30%).

Note. The exotoxin is termed the toxic shock syndrome Toxin-1, and it causes endothelial damage.

SEXUALLY TRANSMITTED DISEASES

STD are infections acquired during sexual intercourse (heterosexual or homosexual), sometimes called venereal diseases. Venus is the Greek Goddess of love. These diseases are caused by:

1. Bacteria. Gonorrhoea, Chlamydial infections including lymphogranuloma venereum, soft sore, granuloma venereum, and mycoplasma infections which lead to cervicitis and salpingitis.
2. Fungi. Tinea cruris and vulvovaginal mycosis (Candidiasis).
3. Spirochetes. Syphilis.
4. Viruses. Human papillomavirus causing condylomata acuminata, genital herpes, hepatitis B, hepatitis C (rare 0.2%), acquired immune deficiency syndrome (AIDS), cytomegalovirus infection and Molluscum contagiosum.
5. Protozoa. Trichomonas vaginitis and amoebiasis of the genital tract.
6. Parasites. Pediculosis pubis and genital scabies.

GONORRHOEA IN THE FEMALE

Causative Organism

Neisseria gonorrhoea which is a Gram-negative intracellular diplococcus.

Mode of Infection

1. Sexual intercourse is responsible for the majority of cases. The incubation period is 2-8 days but may be as long as 2-8 weeks.
2. Contamination from infected towels, instruments ... etc.
3. Neonatal conjunctivitis (ophthalmia neonatorum) may be acquired during vaginal delivery.

Sites of Infection

A. Primary Sites

The gonococci infect the columnar and transitional epithelium (but not stratified squamous epithelium) so the primary sites are: (1) the urethra and skene tubules; (2) the endocervix; (3) the Bartholin glands; (4) the rectum. The vagina is protected in the adult by its thick squamous epithelium and acidic reaction, but it can be infected after abortion, labour, during childhood and after the menopause. Not all the primary sites are affected at the same time.

B. Secondary Sites

Infection may spread along the lumen of the genital tract to affect: (1) endometrium; (2) tubes and ovaries; (3) pelvic peritoneum; (4) bladder or pelvis of the kidney.

C. Systemic Infection with Gonococci

As arthritis, iridocyclitis, hepatitis, meningitis, and gonococcal septicaemia rarely occur.

ACUTE GONORRHOEA

Clinical Picture

Gonorrhoea in women may be asymptomatic, and the clinical picture depends upon the site of infection.

1. **Urethritis.** Frequency and burning micturition. Pus may be milked from the urethra. If a periurethral abscess forms, it is felt through the anterior vaginal wall as a small tender indurated mass.
2. **Acute Cervicitis.** Page 130.
3. **Bartholinitis.** Pain in the region of the gland with oedema of the labium major, the gland is enlarged and tender and abscess formation may occur. The opening of Bartholin duct may appear as a bright red spot known as Sanger macula gonorrhoeica.
4. **Vulvovaginitis.** This occurs in children. There is a purulent vaginal discharge, vulval soreness and pruritus. The inguinal glands may be enlarged and tender.

5. **Pelvic infection.** There are symptoms and signs of acute salpingitis or pelvic peritonitis in severe cases.
6. **Proctitis.** Rectal pain, discharge and may be bleeding.
7. **Gonococcal tonsillitis or pharyngitis.** Occurs as a result of oral sex.
8. **Gonococcal septicaemia** with pyrexia and pustular dermatitis is rare.
9. **The Fitz-Hugh-Curtis syndrome.** It occurs in about 5-10% of cases of acute salpingitis usually gonococcal or chlamydial. The syndrome is characterized by nausea, vomiting, pain in the right hypochondrium, sometimes shoulder pain and positive Murphy sign. It is due to perihepatitis. The organisms reach the perihepatic area from the tubes by lymphatics or by spread along the peritoneal gutters with the circulating peritoneal fluid. Later on perihepatic adhesions form which can cause persistent pain in the right hypochondrium. These "violin string" adhesions between the liver and diaphragm and anterior abdominal wall can be detected by ultrasound scan.

Diagnosis

History of sexual intercourse. Diagnosis does not depend on the clinical picture alone, but the gonococci should be demonstrated by Gram-stained film and culture using modified Thayer-Martin medium. The stained film shows the organisms in only 50% of cases. If culture is positive, we test for antibiotic sensitivity. If culture is not available, the Gonozyne test can be done. It is an enzyme immunoassay test which detects gonococcal antigen. The specimens are taken from cervical canal, the urethra after milking, and by pressing on Bartholin gland.

Treatment

1. Antibiotics

One of the following drugs is given. Ampicillin, erythromycin, or tetracycline 500 mg orally every 6 hours for seven days. Doxycycline (Vibramycin) 100 mg orally twice daily for 7 days. Ciprofloxacin 500 mg in a single oral dose. Azithromycin 1 g in a single oral dose. Spectinomycin (Togamycin) 2 g IM. Gonorrhoea is associated with Chlamydia in 30-50% of cases, and it is advised to give a drug which acts on both microorganisms as erythromycin, tetracycline, doxycycline or azithromycin. Gonococci are resistant to penicillin in 30% of cases. Resistant organisms produce penicillinase enzyme (beta-lactamase). Ampicillin and erythromycin are safe in pregnancy.

2. General Treatment

Avoid sexual intercourse and alcohol intake till the patient is cured. If there is acute salpingitis the patient should rest in bed at hospital.

3. Surgical Treatment

Any abscess as Bartholin abscess should be incised and drained.

Note. When gonorrhoea is suspected or diagnosed we must suspect the presence of other sexually transmitted diseases as Chlamydia, syphilis, AIDS, and hepatitis B.

CHRONIC GONORRHOEA

Clinical Picture

Infection may remain chronic in the urethra, cervical canal or Bartholin gland. Gonococci reaching the tubes die and disappear within 4 weeks after infection and are replaced by other organisms as streptococci and *E. coli*, especially from the bowel. The clinical picture depends upon the site of infection so there may be evidence of chronic urethritis, chronic cervicitis or chronic salpingo-oophoritis. The Bartholin gland may be enlarged and tender, or it may be the site of recurrent abscess or cyst formation. In some cases (50%) chronic gonorrhoea is asymptomatic.

Diagnosis

The diagnosis is proved by demonstrating the gonococci in smear and culture. Culture is essential for diagnosis.

Treatment

An antibiotic to which the organism is sensitive is given and any residual lesion is treated according to its nature, e.g. cauterization for chronic cervicitis.

GENITAL CHLAMYDIAL INFECTIONS

Causative Organism

Chlamydia trachomatis is an intracellular Gram-negative bacterium. There are several serotypes. Serotypes A, B and C are associated with trachoma. Serotypes D to K lead to genital infections in male and female. Serotypes L1, L2 and L3 cause lymphogranuloma venereum.

Mode of Infection

1. Sexual intercourse. The incubation period is 7-14 days. It is the most common sexually transmitted disease in Sweden, the United States, and many European countries.
2. Neonatal conjunctivitis results from transmission of organisms to the eyes during vaginal delivery (similar to gonococcus).

Clinical Picture

1. *C. trachomatis* is asymptomatic in about 75% of cases.
2. Like gonococci the organism infects the columnar and transitional epithelium and ascends along the lumen of the genital tract. It leads to urethritis, Bartholinitis, cervicitis, endometritis, salpingitis, peritonitis, proctitis and perihepatitis (Fitz-Hugh-Curtis syndrome).
3. Infertility.

4. During pregnancy the infection may cause abortion, preterm labour, premature rupture of membranes and postpartum endometritis. The newborn may acquire inclusion conjunctivitis, otitis media and pneumonia during vaginal delivery.

Diagnosis

The diagnosis is confirmed by one of the following tests:

1. Tissue culture which is the most reliable method. Discharge from the lesion is cultured on specific medium (MacCoy medium).
2. Examination of urethral or cervical discharge or other clinical material with Giemsa stain. It will show the intracellular bacterium.
3. Testing the maternal serum for antichlamydial antibodies. Unreliable because of the high false positive result.
4. Detection of chlamydial antigen in any clinical material by one of the following methods:
 - a. The immunofluorescent-stained smear.
 - b. The ELISA test (enzyme linked-immunosorbent assay).
 - c. The DNA probe test. Reliable as culture.
 - d. The polymerase chain reaction (PCR) test. More rapid and more sensitive than culture.
 - e. The lipase chain reaction (LCR) test which is done on urine.

Note. The polymerase chain reaction is a process by which small fragments of DNA are cloned to produce larger amounts of DNA suitable for analysis. PCR, or LCR can be used as a screening test, e.g. a person with more than one sexual partner.

Treatment

C. trachomatis is sensitive to tetracycline and erythromycin. The dose is 500 mg orally every 6 hours for 7 days. The husband should be treated at the same time. In lymphogranuloma venereum the drug is given for 21 days. Other drugs as doxycycline and clindamycin can be given. Also azithromycin 1 g in a single oral dose. Erythromycin is safe during pregnancy,

SYPHILIS

Syphilis is caused by *Treponema pallidum* which is found in all lesions primary, secondary and tertiary. The disease is congenital or acquired.

Clinical Picture

Primary Stage

The primary lesion or chancre appears on the mucosa of the lower genital tract (cervix, vagina, clitoris, labium major, labium minor, fourchette) and urethra. The chancre may appear on other areas as the lips, mouth (oral sex) or anorectal region. Incubation period is 10-90 days. The chancre appears as a solitary, non-tender, indurated ulcer. In 10% of cases more than one chancre is present. The chancre usually heals after 1-6 weeks. The inguinal glands

enlarge when the lesion is on the vulva or lower vagina. They are hard, not tender and do not suppurate.

Secondary Stage

If untreated, the manifestations of secondary syphilis appear in 6 weeks to 6 months after healing of the chancre. These result from entry of spirochetes into the bloodstream and include pyrexia, condylomata lata, generalized lymphadenopathy and occasional loss of scalp hair. The condylomata appear as flat wart-like growths on the vulva and around the anus. Sometimes the secondary lesions appear before healing of the chancre or they may not occur at all. The patient is a source of infection during the first and second stages of the disease.

Tertiary Stage

It is characterized by the formation of gummas in any part of the body.



Fig.58. Chancre

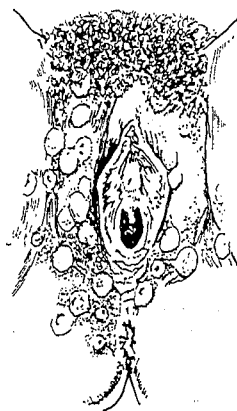


Fig.59. Condylomata lata

Diagnosis

The material obtained from primary or secondary lesions is examined by dark-field microscopy to detect spirochetes. The serological tests for syphilis include 2 groups. The first group are nonspecific or nontreponemal tests as the Wasserman reaction test (WR), the Venereal Disease Research Laboratory test (VDRL) and Rapid Plasma Reagin test (RPR). The specific or treponemal tests include the treponema pallidum immobilization test and the fluorescent treponemal antibody absorption test (FTA-ABS). A nonspecific test e.g. VDRL is performed and if positive a specific treponemal test is done to confirm or to exclude the diagnosis of syphilis. The serological test starts to be positive 2 weeks after appearance of the chancre and may be negative in very late syphilis.

Notes

- Dark-field microscopy rather than normal-light microscopy is used for detection of spirochetes because they are very thin.

- The nonspecific tests detect the presence of anticardiolipin antibodies. Cardiolipin is a nonspecific antigen produced during syphilitic infection as well as other pathological conditions as rheumatoid arthritis and lymphomas.

Treatment

I. Primary and Secondary Syphilis

- Procaine penicillin 600,000 units IM daily for 10 days or the long-acting benzathine penicillin 2.4 million units IM (half the dose in each buttock).
- For patients allergic to penicillin; oral erythromycin, tetracycline or cephalosporin 500 mg 6 hourly for 15 days.

II. All Other Syphilis

(Latent, gummatous, neuro and cardiovascular)

- Procaine penicillin 600,000 units IM daily for 20 days or benzathine penicillin 2.4 million units IM weekly for 3 weeks. The long-acting penicillin is contraindicated in neurosyphilis because it does not reach enough concentration in the cerebrospinal fluid.
- For patients allergic to penicillin; oral erythromycin, tetracycline or cephalosporin 500 mg 6 hourly for 30 days.

Note. Tetracyclines should not be prescribed in pregnancy because they cause discolouration of the fetal deciduous teeth.

CONDYLOMATA ACUMINATA

Causative Organism

Genital warts are caused by the human papillomavirus (Papova virus). More than 100 subtypes have been identified. About 35 subtypes infect the female genital tract.

Mode of Infection

The virus is transmitted by sexual intercourse, but can be transferred to the genital area from other parts of the body by direct contact, by fingers, or by instruments. It can be transmitted to the fetus during pregnancy (trans-placental) or during delivery leading to genital or laryngeal papillomata.

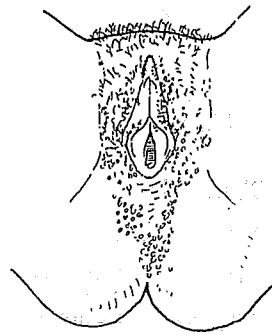


Fig.60. Condylomata acuminata

Clinical Picture

- There are multiple small papillomata which usually grow in groups, rarely single. The warts appear on the vulva and around the anus and can affect the vagina, cervix, anal canal and lower part of the rectum. Heat and moisture stimulate the growth of warts.

2. The condylomata grow more rapidly in women who are pregnant, diabetic, on combined oral contraceptives, and on immunosuppressant therapy. Decreased immunity in pregnancy and hormonal changes stimulate the growth of the lesion.
3. The human papillomavirus predisposes to carcinoma of the vulva, vagina, cervix and anorectal region.

Investigations

1. Cytology using Papanicolaou smear shows characteristic cells known as koilocytes. The koilocyte is a large cell with a large hyperchromatic wrinkled nucleus, with a perinuclear halo.
2. Biopsy taken from the lesion for histopathological examination.
3. Colposcopic examination of the cervix and vagina.

Treatment

1. Small lesions less than 2 cm in diameter are painted with 25% podophyllin resin in liquid paraffin. The surrounding normal skin is covered with a protective as vaseline. The patient is instructed to wash the treated area after 4-8 hours to remove the medication which causes ischaemia and necrosis of the warts. Podophyllin is contraindicated in pregnancy because it is absorbed from the skin and can lead to abortion, preterm labour, congenital malformation and fetal death. Trichloroacetic acid solution, and 5-fluorouracil cream 5% can be used.
2. Large lesions are treated by surgical removal, cryocautery, diathermy coagulation or laser vaporization. For cryocautery we use a spray of liquid nitrogen, or a metal probe cooled with liquid nitrogen.
3. The use of immunomodulator drugs:
 - a. Alpha-interferon; given systemically, inside the lesion, or as topical cream.
 - b. Imiquimod. A topical cream which elevates interferon levels.
 - c. Inosine probonex taken orally.

GENITAL HERPES

Most cases follow infection with Herpes simplex virus type 2. Infection with type 1 usually follows oral sex. Both have the same clinical picture. Incubation period is 3-7 days, but may be up to several weeks. The lesion affects the lower genital tract (cervix, vagina and vulva) perianal area and rectum. Vesicles appear which break down into multiple, small, shallow, very painful ulcers. There is erythema, discharge, oedema, and the inguinal nodes are often enlarged. Healing usually occurs by tenth day. Recurrence of infection is common as the virus remains quiescent in the sacral ganglia. The clinical picture suggests the diagnosis but this should be confirmed by tissue culture for the virus or by the polymerase chain reaction test, or DNA probe test.

Treatment. Aciclovir (Zovirax) oral tablets, one tablet (200 mg) 5 times daily for 5 days (1×5×5). Aciclovir is given intravenously in severe cases. In mild and recurrent disease aciclovir cream may be enough. It is applied 5 times daily for 5 days. Other drugs used are valaciclovir, and famciclovir.

LYMPHOGRANULOMA VENEREUM

LGV or LG inguinale is caused by *Chlamydia trachomatis* (serotypes L1, L2, L3). Incubation period is 7-14 days. The lesion starts as papules or vesicles on the vulva and may be around the anus which break down to form ulcers. The disease spreads by lymphatics causing inguinal adenitis. The nodes are matted together and tend to breakdown to form multiple abscesses. Chronic lymphatic obstruction can result in vulval elephantiasis. Rectal strictures and fistulas are frequent. The diagnosis is made by one of the tests mentioned with chlamydial genital infections. Treatment is by oral tetracycline or erythromycin 500 mg 6-hourly for 21 days. Other drugs as doxycycline, clindamycin, and azithromycin can be used. Suppurating inguinal lymph nodes (Bubos) are aspirated as incision is contraindicated.

GRANULOMA VENEREUM (INGUINALE) (DONOVANOSIS)

Infection is caused by a Gram-negative bacillus- *Calymmatobacterium granulomatis*. The bacilli appear as intracellular bodies known as Donovan bodies. Incubation period is 10-40 days. The lesion involves the vulva and less frequently the vagina and perineum. The lesion starts as papules or vesicles which break down to form ulcers. The inguinal glands enlarge but do not suppurate and this differentiates the lesion from LGV. Diagnosed by demonstration of Donovan bodies in exudate obtained from the ulcer by using the Giemsa stain. Treatment is by oral tetracycline or erythromycin 500 mg 6 hourly for 21 days.

SOFT SORE (SOFT CHANCER, CHANCROID)

Infection is caused by a Gram-negative bacillus-*Haemophilus ducreyii*. Incubation period is 2-5 days. The lesion takes the form of multiple small papules or vesicles which break down to form very painful shallow ulcers which are usually multiple but can be single and are found on the vulva and may be around the anus. It may also involve the vagina, cervix or urethra. The inguinal lymph nodes are tender and become matted to form an abscess. The diagnosis is confirmed by demonstrating the bacilli in the discharge from the ulcer or in the pus aspirated from an inguinal node using Gram stain and culture. Treated with sulphonamides and if this fails we give tetracycline, erythromycin or chloramphenicol. Also azithromycin 1 g in a single oral dose.

AIDS

The acquired immune deficiency syndrome is caused by the human immune deficiency virus (HIV). The virus is present in the blood, semen and saliva of affected individuals. The mode of infection is by sexual intercourse, blood transfusion, blood products, infected

syringes, instruments, and maternofetal (vertical) transmission which occurs in about 30% of pregnancies. The virus destroys the T-lymphocytes and thus reduces immunity and results in the development of life threatening infections and unusual malignant lesions or both. It is treated by giving 2 drugs in mild cases and 3 drugs in severe cases. Examples are zidovudine and lamivudine. However, no specific medication is yet available.

Note. Vertical transmission of HIV occurs antenatally through the placenta, intranatally during passage in the birth canal if the fetus is injured, and postnatally through the milk during lactation. So breast-feeding is contraindicated.

AMOEBIASIS

The parasite *Entameba histolytica* spreads from the rectum to cause ulcerative lesions in the vagina, cervix and endometrium. Patient may complain of blood stained vaginal discharge. Diagnosis is made by demonstration of the parasite in stools and vaginal discharge and biopsy specimens. Treated by metronidazole (Flagyl) 500 mg TDS for 5-10 days.

TUBERCULOSIS OF THE FEMALE GENITAL ORGANS

In the majority of cases, infection is secondary to a tuberculous lesion elsewhere in the body as the lungs or bowel. In very few cases, primary infection occurs by tuberculous semen or sputum. The human bacillus (*Mycobacterium tuberculosis*) is responsible for most cases. Occasionally the bovine bacillus (*Mycobacterium bovis*) causes human disease. The portal of entry of the human bacillus is the lung as an airborne infection. The portal of entry of the bovine bacillus is the intestine through infected cattle milk.

Prevalence

It varies greatly according to the socio-economic conditions. In the USA less than 1% of infertile women have genital tuberculosis, and in India the figure is 13%.

Mode of Infection

1. Spread by blood or lymph from a primary lesion elsewhere in the body as the lungs or bronchial lymph glands (bloodstream) or mesenteric lymph nodes (by lymphatics).
2. Direct spread from tuberculous peritonitis or tuberculous mesenteric glands.
3. Ascending infection with tuberculous semen or sputum.

Pathology

Tuberculosis of the Tube

The tubes are affected in more than 90% of cases of genital tuberculosis. The infection is bilateral in the majority of cases. Infection may be in the form of:

- a. **Tuberculous perisalpingitis.** Miliary tubercles appear on the peritoneal coat of the tube. It is a part of tuberculous pelvic peritonitis.
- b. **Tuberculous interstitial salpingitis.** The wall of the tube is thick and fibrous. The muscle layer shows caseous foci. The tube is tortuous and surrounded by adhesions.

Infection occurs by the bloodstream. In some cases nodules appear in the region of the isthmus while the rest of the tube is free. This is called salpingitis isthmica nodosa.

- c. **Tuberculous endosalpingitis.** Infection starts in the mucosa which becomes infiltrated and necrotic. The tube may become distended by thick caseous material forming a tuberculous pyosalpinx. At operation tuberculous pyosalpinx is recognised by: (1) pallor of the tissue because of endarteritis obliterans; (2) dense adhesions; (3) tubercles may be seen on the peritoneal coat; (4) the organ is usually sausage-shaped and not retort-shaped because distension usually starts at the isthmical end; (5) in many cases the abdominal ostium remains patent (50%); (6) calcification may be seen in the wall; (7) the presence of small nodules at the isthmus; (8) caseous nature of the contents.



Fig.61. Tuberculous pyosalpinx

- d. In some cases the tube appears normal and evidence of tuberculosis is only found on microscopical examination.

Tuberculosis of the Uterine Body

This occurs in about 45% of cases. Infection is always secondary to a tubal lesion. In early cases tubercles appear in the endometrium near one or both cornua or in the region of internal os (gravitation). Gradually, the endometrium becomes replaced by tuberculous granulation tissue. Tuberculous pyometra may result. In advanced cases, the myometrium becomes involved.

Tuberculosis of the Ovaries

Occurs in about 30% of cases mostly as a direct extension from the tube. The ovary may look normal on naked eye appearance, however, the disease may be manifested by surface tubercles, extensive adhesions, or tuberculous abscesses.

Tuberculosis of the Cervix

In 10% of cases. The lesion takes the form of polypi or ulcers. Tuberculous ulcers are single or multiple. The ulcer has a serpiginous outline, undermined edge and a yellow floor. The base is soft and so it looks like carcinoma but feels like an erosion.

Tuberculosis of the Vagina and Vulva

Very rare about 1% of cases. The lesion takes the form of polypi or ulcers.

Diagnosis

The possibility of tuberculosis is suspected in the following cases: family history of tuberculosis, history of exposure to infection, patient coming from an endemic area, idiopathic infertility, chronic pelvic infection in a virgin or which is resistant to treatment.

Symptoms

The condition may be asymptomatic, however, the patient may complain of one or more of the following:

1. Infertility, the commonest complaint. It is due to anovulation resulting from ovarian tuberculosis and bad general condition, blocked tubes, and destruction of the endometrium preventing implantation of the ovum.
2. Pain in the form of dull ache in the lower abdomen. Tuberculous lesions in the vulva cause severe pain.
3. Symptoms of pelvic congestion in the form of congestive dysmenorrhoea, menorrhagia and increased normal vaginal discharge (leucorrhoea). The vaginal discharge may be blood stained due to the presence of ulceration in the cervix or vagina.
4. Menstrual disturbances. Oligomenorrhoea and amenorrhoea. Amenorrhoea is due to bad general condition of the patient, destruction of the endometrium or ovaries, also the tuberculous toxins inactivate oestrogens. Menorrhagia, metrorrhagia, and postmenopausal bleeding may occur.
5. General symptoms of tuberculosis may be present in the form of loss of appetite, loss of weight, excessive sweating and afternoon fever.

Signs

General Examination

This may reveal a tuberculous lesion elsewhere in the body as the lungs.

Abdominal Examination

It may show tuberculous peritonitis.

Vaginal Examination

(a) Inspection for tuberculous lesions in the vulva; (b) bimanual examination: the uterus feels normal or slightly enlarged, the tubes are normal, thickened or an adnexal swelling is felt which is fixed, tender and indurated. Small nodules may be felt in Douglas pouch; (c) speculum examination reveals lesions in the cervix or vagina.

Investigations

1. Blood picture. Anaemia, leucopenia with relative lymphocytosis and high sedimentation rate.
2. Tuberculin test. If negative it excludes tuberculosis.
3. X-ray to the chest to detect an active primary focus.

4. Pelvic sonography. It may show adnexal masses with scattered small calcification which is highly suggestive of tuberculous infection.
5. Premenstrual endometrial biopsy. This is examined by stained film (Ziehl Neelsen stain) and culture on specific media as Lowenstein-Jensen (L-J) or MGIT medium. The menstrual blood can be examined in the same way.
6. Biopsy from lesions in the cervix, vagina and vulva.
7. Molecular diagnosis by PCR or MTD test done on any clinical specimen.
8. Laparoscopy, when done to investigate infertility, will show tubercles on the peritoneal coat. Tuberculous pyosalpinx has certain features. See above.
9. Hysterosalpingography. It is not done if genital tuberculosis is suspected, as it may cause exacerbation of the infection. However, if it is carried out to investigate a case of infertility, the presence of certain signs suggests tuberculosis and include: (a) the tubes appear straight with rigid outlines (pipe stem or lead pipe appearance) with localized dilatations (beading); (b) calcification of the tubal wall; (c) obstruction of the tube is bilateral in the majority of cases; (d) saw-toothed outline of the opaque shadow in the tubes or uterine cavity denoting multiple ulcerations of the mucosal lining; (e) the uterine cavity may be deformed with intrauterine adhesions; (f) the occurrence of intravasation is strongly suggestive of tuberculous endometritis. Intravasation means the presence of the dye in pelvic veins or lymphatics.

Note. MGIT medium = mycobacterium growth indicator test medium.
 MTD test = mycobacterium tuberculosis detection test.

Treatment

A. Medical

1. Admission to hospital may be indicated when an active extragenital lesion is present as well.
2. Nourishing diet, tonics and vitamins.
3. Chemotherapy. The following treatment is given for 9 months.

Three drugs are given for 2 months: ethambutol or streptomycin plus isoniazid plus rifampicin. This is followed by isoniazid and rifampicin given for 7 months (Rifinan is a combined tablet containing these 2 drugs).

Doses. Streptomycin 1 gm IM/day. All other drugs are given orally. Ethambutol: 15 mg/kg body weight/day. Isoniazid (isonicotinic acid hydrazide): 300 mg/day. Rifampicin: 450 mg/day if the weight of the patient is below 50 kg and 600 mg/day if the weight is more than 50 kg.

Note. There are other regimens given for 6 and 12 months.

B. Surgical

Indicated if medical treatment fails and in the presence of large masses. For tuberculous adnexa we do total hysterectomy and bilateral salpingo-oophorectomy. Surgery is preceded

and followed by chemotherapy for at least 3 months. Drains should not be used to avoid fistula formation.

Prognosis

The pregnancy rate after medical treatment is 20% however, one third will abort, in one third ectopic pregnancy occurs and one third will continue to full term.

Note for the postgraduate

Tubercles on peritoneal surfaces may be caused by tuberculosis, bilharziasis, malignancy, oil granulomata following hysterosalpingography when lipiodol is used, and talc powder granulomata from surgical gloves used in a previous laparotomy.

BILHARZIASIS OF THE FEMALE GENITAL TRACT

Pathology

Infection is caused by *Schistosoma haematobium*, however, in few cases it is caused by *Sch. mansoni*. The ova are deposited in the submucous or subcutaneous tissues with formation of bilharzial granulation tissue. The lesion takes the form of papillomata or ulcers. In late cases fibrosis occurs. Calcification may occur in longstanding lesions. The commonest sites affected are the vulva, vagina and portio vaginalis of the cervix.

Clinical Picture

Bilharziasis of the Vulva

Any area of the vulva or the perineum can be affected. The lesion takes the form of papillomata or ulcers. The papillomata are small, sessile, firm, and usually multiple. They are dark red in colour with occasional areas of calcification. The presence of multiple papillomata leads to pseudo-elephantiasis. Bilharziasis of the hymen leads to its thickening. The ulcers are superficial and multiple. Vulval lesions are mostly seen in children. Symptoms include itching, pain, discharge, and bleeding.

Bilharziasis of the Vagina

This appears in the form of multiple papillomata, ulcers, sandy patches giving rise to granular vaginitis or vaginal stenosis due to fibrosis. The symptoms are vaginal discharge, irregular vaginal bleeding, and dyspareunia.

Note. Sandy patches are calcified ova beneath the mucous membrane.

Bilharziasis of the Cervix

The portio vaginalis of the cervix is the commonest site of genital bilharziasis. The lesion takes the form of ulcers or papillomata which may be single or multiple. The main symptoms are vaginal discharge, irregular vaginal bleeding and infertility. Bilharzial antibodies are spermatotoxic.

Bilharziasis of the Uterine Body

It may affect the endometrium or myometrium. Irregular uterine bleeding is the main symptom. The lesion is very rare due to monthly shedding of the endometrium.

Bilharziasis of the Tubes and Ovaries

Usually bilateral. Lesion in the tube may be localized (salpingitis isthmica nodosa) or diffuse and predisposes to ectopic pregnancy. The ovary is usually enlarged with thickened tunica albuginea and may show hard nodules on the surface. The main symptoms are lower abdominal pain, congestive dysmenorrhoea and infertility (blocked tubes).

Diagnosis

Young age of the patient. Residence in an endemic area. History of terminal haematuria. Symptoms and signs suggestive of bilharziasis. Urine and stool analysis. Cystoscopy and proctoscopy. Demonstration of bilharzial ova by biopsy, vaginal smear or scraping from ulcers. Bilharzial ova can be seen through the colposcope. Complement fixation and precipitation tests.

Complications

(1) Urinary fistulae, (2) infertility. There is no proof that bilharziasis predisposes to carcinoma of vulva, vagina, or cervix.

Treatment

(1) Antibilharzial drugs as Ambilhar and Biltricide oral tablets. Biltricide is given as a single oral dose, 40 mg/kg body weight; (2) antibiotics if there is secondary infection; (3) treatment of associated anaemia; (4) surgical excision of residual lesions.

ACTINOMYCOSIS

It is a fungus infection. The Actinomycetes, most often *Actinomyces Israelii* can cause acute or chronic infection in the tube or ovary. The organism is a normal commensal of the mouth and gut. Infection occurs by direct spread from ruptured appendix or perforated colon. Also the presence of intrauterine contraceptive device can lead to ascent of organisms from the vagina to reach the tubes or ovaries. Organisms reach the vagina from the rectum. Infection can lead to a tubal or ovarian inflammatory mass. Treated by penicillin, tetracycline or erythromycin. If the pelvic mass does not respond to antibiotics, surgical excision is performed.

VAGINAL DISCHARGE AND LEUCORRHOEA

Leucorrhoea means the flow of a white substance and it is used to indicate an increased amount of the normal vaginal discharge. Sometimes, the term is used to indicate all abnormal vaginal discharges except blood.

THE NORMAL VAGINAL DISCHARGE

Normally, the vulva and vagina are kept moist by a discharge derived from the following sources:

1. **Vulva.** The Bartholin glands secrete alkaline mucus during sexual stimulation. Secretion from Skene tubules contributes to lubrication of the vulva.
2. **Vagina.** It contains no glands but it is kept moist by a serous transudate from its walls which is acidic in reaction due to the presence of lactic acid (pH 3.5-4.5).
3. **Cervix.** The endocervix secretes alkaline mucous discharge (pH 8.5) which plugs the cervical canal and prevents ascent of infection. Oestrogen increases the amount and fluidity of cervical secretion.
4. **Endometrium.** It secretes an alkaline fluid rich in glycogen, glucose and fructose during the secretory phase of the cycle (uterine milk).
5. **The tubes.** Secrete a serous fluid rich in proteins and may reach the vagina at times.

AETIOLOGY OF VAGINAL DISCHARGE

I. Physiological Discharge

Increased normal discharge, that is true leucorrhoea occurs in the following conditions:

1. At puberty due to increased vascularity of genital organs and unopposed oestrogenic stimulation. The increased discharge may occur a few years before or after menarche and it is temporary and corrects itself.
2. At ovulation due to increased cervical secretion (effect of oestrogen).
3. Premenstrual due to pelvic congestion and increased secretion of endometrial glands.
4. Postmenstrual from the healing endometrial surface.
5. Pregnancy because of hyperaemia and hyperoestrinism.
6. Pelvic congestion due to any cause as constipation and retroversion.
7. Sexual excitement due to Bartholin gland secretion.
8. Hormonal non-infected cervical erosion because the columnar epithelium of the erosion secretes mucus.
9. Vaginal adenomatosis. Columnar epithelium replaces the squamous lining of the vagina. This epithelium is cervical in type and secretes mucus.
10. The oestrogen-progestogen contraceptive tablet.

II. Pathological Discharge

1. Lesions in the Vagina

- All types of vaginitis, especially due to Monilia, Trichomonas, and Bacterial vaginosis.
- Ulcers of the vagina which may be traumatic, chemical, inflammatory, neoplastic and postirradiation.
- Tumours of the vagina.
- Retained foreign body or neglected pessary.
- Abnormal communications with the vagina as vesicovaginal and rectovaginal fistulae.

2. Lesions in the Cervix

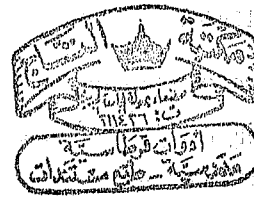
- Cervicitis and infected erosion.
- Ulcers of the cervix.
- Tumours and polypi of the cervix.

3. Uterine Causes

Endometritis (puerperal, tuberculous, bilharzial and senile), benign and malignant tumours and intrauterine contraceptive device.

4. Tubal Causes

- Intermittent hydrosalpinx.
- Tumours.



INVESTIGATION OF A CASE OF VAGINAL DISCHARGE

A. History

- Age. The commonest causes of vaginal discharge in children are vulvovaginitis, foreign body and oxyuris infection. The commonest causes in adult life are bacterial vaginosis, monilial and trichomonal vaginitis. After menopause the commonest causes are senile vaginitis, senile endometritis and malignant lesions.
- Marital state for the possibility of sexually transmitted diseases as Trichomonas vaginitis and gonococcal cervicitis.
- Menstrual history. The date of last menstruation to exclude pregnancy.
- Obstetric history. If the discharge starts after abortion or labour it is usually due to cervical infection.
- Present history. The duration, amount, character and odour of the discharge and its relation to menstruation. Symptoms of trichomonas infection often begin during or after menstruation (organism needs low acid medium).
- The presence of other symptoms as pruritus vulvae, dyspareunia, and urinary symptoms.

B. General Examination

For evidence of cachexia (malignant lesion).

C. Abdominal Examination

For a pelvi-abdominal swelling as fibroid or pregnancy.

D. Pelvic Examination

The patient should not have a vaginal douche for at least 2 days before examination and has not used any vaginal medication for at least 5 days. The speculum and gloves must be sterile and dry. We must avoid any antiseptic or lubricant.

1. Inspection of the vulva; for vulvitis, Bartholinitis and the presence of discharge.
2. A speculum is introduced and the discharge collected in the posterior fornix is examined for the amount, character, and the presence of froth or blood. The pH of discharge is estimated by a universal indicator. A drop of discharge is taken, put on a slide and a drop of normal warm saline is added then examined microscopically for *Trichomonas vaginalis*, clue cells of Bacterial vaginosis and *Candida* organism. Another drop is taken for a Gram-stained film and a third drop is taken for culture. Finally, the cervix and vagina are dried and inspected for any lesion.
3. The urethra is milked and discharge obtained is examined by Gram-stained film and culture.
4. Bimanual examination is performed to detect a lesion in the uterus or adnexa.

Special Investigations

These are done according to the clinical findings.

1. Urine for sugar and bilharzial ova. Diabetes mellitus must be excluded in monilial vaginitis.
2. Stool analysis for oxyuris infection.
3. Serological test for syphilis if suspected.
4. Investigations to exclude malignancy; including cervical smear and biopsy from suspected lesions.
5. In infants, an X-ray or ultrasound may be done to exclude a foreign body.

Treatment

It is the treatment of the cause.

Note. Döderlein bacilli live on glycogen present in exfoliated vaginal epithelial cells. The organisms breakdown glycogen into lactic acid which maintains the acidic reaction of the vagina. The growth of pathogenic organisms diminishes the glycogen content in the vagina which in turn inhibits the growth of Döderlein bacilli.

SECTION VII

INFERTILITY AND CONTRACEPTION

INFERTILITY (العقر) AND STERILITY (العقم)

Infertility means inability to conceive after one year of regular intercourse, without the use of contraception. Primary infertility means conception has never occurred. Secondary infertility means failure of conception after one or more pregnancy. Sterility is inability to conceive due to a cause which cannot be treated as absence of uterus. 10-15% of married couples are infertile.

CAUSES OF INFERTILITY

A. Causes in the Female

1. Ovarian Factor (30-40% of female causes). Anovulation, oligo-ovulation and luteal phase defect (LPD). The latter leads to poor secretory changes in the endometrium which prevent implantation of the fertilized ovum (or causes early abortion).
2. Pelvic Adhesions. These prevent the passage of the ovum from the ovary to the tube. This occurs with pelvic peritonitis of any kind and with pelvic endometriosis.
3. Bilateral Tubal Obstruction (30-40%). This may be:
 - a. Congenital as long and narrow tubes and non-canalization.
 - b. Traumatic. Surgical removal and postoperative adhesions.
 - c. Inflammatory. Chronic salpingitis due to any cause.
 - d. Neoplastic. The presence of bilateral cornual fibroids.
 - e. Functional due to uterotubal spasm.
4. Uterine Factor (5-10%).
 - a. Congenital. Absence or marked hypoplasia of the uterus. Uterine anomalies as bicornuate and septate uterus are more often associated with abortion than with infertility.
 - b. Traumatic. The presence of intrauterine adhesions (Asherman syndrome).
 - c. Inflammatory due to tuberculous endometritis.
 - d. Neoplastic caused by the presence of fibroids.
 - e. Functional. The presence of refractory (unresponsive) endometrium due to absence of progesterone receptors which is very rare.
5. Cervical Factor (5-10%).
 - a. Congenital atresia and congenital elongation of the portio vaginalis.
 - b. Traumatic. Cauterization leading to fibrosis and cervical stenosis and destruction of the endocervical secretory cells, so the cervical mucus becomes scanty and thick

(hostile) preventing ascent of spermatozoa. Conization removing the secretory cells, and excessive cervical amputation which decreases the amount of mucus.

- c. Inflammatory. Chronic cervicitis destroys the secretory cells, also pus cells affect sperm motility and migration.
- d. Neoplastic. A cervical fibroid causes mechanical obstruction.
- e. Functional. Increased viscosity of cervical mucus caused by oestrogen deficiency, and clomiphene (Clomid) therapy.
- f. Abnormal direction of the cervix in uterine prolapse and retroversion.
- g. Immunological. The presence of antisperm antibodies in the cervical mucus leading to agglutination or immobilization of sperms.

Note. The causes of hostile cervical mucus are: chronic cervicitis, cauterization, conization, excessive amputation, clomiphene therapy, presence of antisperm antibodies, oestrogen deficiency, and acidic cervical mucus.

6. Vaginal Factors (1%).

- a. Congenital. Aplasia and hypoplasia interfering with sexual intercourse and the presence of a transverse vaginal septum.
- b. Traumatic. Vaginal operations as anterior or posterior repair may lead to narrowing of the vagina or the presence of a tender scar resulting in dyspareunia.
- c. Inflammatory. Vaginitis with purulent discharge as in Trichomonas infection.
- d. Neoplastic. Tumours or cysts interfering with intercourse.
- e. Functional. The presence of vaginismus.
- f. High vaginal acidity killing the spermatozoa.

B. Causes in the Male

1. Abnormal semen such as:

- a. A volume less than 2 ml or greater than 7 ml. A volume < 2 ml may be too small to allow adequate contact with the cervix. A volume > 7 ml dilutes sperm concentration, so that insufficient number comes in contact with the cervix.
- b. Azoospermia. Complete absence of spermatozoa in the seminal fluid.
- c. Oligospermia. Marked diminution in the number of spermatozoa to be less than 20,000 per cubic millimeter.
- d. Polyspermia. Marked increase in the number of spermatozoa to be more than 250,000 per cubic millimeter. This reduces fertility.
- e. Necrospermia. All spermatozoa are dead.
- f. Asthenospermia. Reduction or loss of motility of spermatozoa.
- g. Abnormal forms of spermatozoa 70% or more. Increased number of abnormal forms is called teratospermia.
- h. Increased viscosity. Semen does not liquefy within half an hour at room temperature.
- i. Agglutination. More than 10% of sperms show agglutination (head to head, tail to tail, or head to tail). This is suggestive, but not conclusive of an immunological cause.

- j. Number of round cells more than 5 millions/ml. Round cells include leucocytes (pus cells) and immature spermatogenic cells (spermatogonia, spermatocytes, and spermatids).
- k. Presence of pus cells (pyospermia) more than one million/ml.
- l. Low fructose or low prostaglandin content may be a factor (fructose is essential for metabolism and prostaglandin for motility of spermatozoa).
- 2. Bilateral obstruction of the epididymis, vas deferens or ejaculatory ducts.
- 3. Failure to deposit semen in the vagina due to impotence, premature ejaculation before penetration, hypospadias, phimosis, or retrograde ejaculation in the bladder which occurs after prostatectomy.

Note. Fructose and prostaglandins come from seminal vesicles. Normal semen fructose level is 120-240 mg%.

C. Coital Errors

(1) Aparentia and dyspareunia; (2) vaginismus; (3) fluor seminis which means abnormal escape of semen from the vagina after coitus; (4) infrequent intercourse, so the time of coitus does not coincide with ovulation. Coitus needs to take place every other day during the fertile period to give the best chance for conception. Also, too frequent intercourse may lead to infertility, as this may lead to production of immature sperms, and reduces the volume of semen and number of sperms coming in contact with the cervix; (5) vaginal washing immediately after intercourse washes away the sperms; (6) the use of a lubricant when coitus is difficult, or the vagina is dry. This interferes with sperm motility and migration.

D. Immunological Factors

The wife may produce antibodies against her husband spermatozoa leading to infertility, or the husband may produce antibodies against his own sperms (autoimmune disease). These autoantibodies either cause azoospermia or agglutinate or immobilize the sperms after ejaculation.

E. Idiopathic

No cause is found to explain infertility in about 10% of cases.

Notes

1. The wife may produce antibodies against her husband spermatozoa if breaks are present in the vaginal mucosa. This allows exposure of the wife to sperm proteins (antigen) leading to production of antibodies. When these antibodies are present in the cervical mucus they lead to immobilization or agglutination of the sperms leading to infertility. The antisperm antibodies are of 2 types, IgM and IgG antibodies. IgM antibodies have large molecules and are present only in serum as they cannot cross the wall of blood vessels. Cervical mucus contains only IgG antibodies.
2. If semen analysis is abnormal or borderline, it should be repeated after at least 2 weeks.

INVESTIGATION OF A CASE OF INFERTILITY

In about 30% of cases the cause is in the female, in 30% the cause is in the male, in 30% there is a cause both in the male and female and in 10% of cases no cause is found. So the sterile couple must be investigated together as one unit. The husband must be investigated, even if he is responsible for one or more pregnancy, because he may be subfertile, or might have acquired a disease, that makes him infertile.

Investigation of the Wife

A. History

1. Personal history. Age, duration of marriage, previous marriage, occupation and special habits as smoking and alcohol intake.
2. Menstrual history in detail, including any change in the menstrual cycle.
3. Obstetric history in case of secondary infertility. History of septic abortion, or puerperal sepsis. Details of any operative delivery.
4. Past history. (a) Diseases as gonorrhoea or other sexually transmitted diseases, tuberculosis, mumps, diabetes mellitus and appendicitis; (b) operation on the genital tract as myomectomy; (c) previous X-ray treatment; (d) any hormonal treatment; (e) previous investigations or treatment carried out for the couple.
5. Family history of diabetes mellitus and tuberculosis.
6. Sexual history. (a) Frequency of intercourse; (b) the presence of apareunia or dyspareunia; (c) fluor seminis; (d) the occurrence of orgasm. Female orgasm is not essential for conception because pregnancy can occur in case of rape, but orgasm increases the chance by increasing the amount of cervical secretion and by abolishing any uterotubal spasm; (e) vaginal washing immediately after intercourse which is a frequent habit among Egyptian females; (f) the use of a lubricant during coitus; (g) the previous use of any contraception.

B. General Examination

(1) The general state of health; (2) examination of thyroid, breasts for galactorrhoea, chest and heart; (3) presence of secondary sex characters; (4) distribution of hair and fat.

C. Abdominal Examination

For a pelvi-abdominal swelling, e.g. fibroid.

D. Pelvic Examination

To detect abnormality in the pelvic organs as uterine hypoplasia. A uterine sound is passed, if the cervix looks stenosed.

If the patient is clinically free, she is subjected to further investigations but after excluding the husband as a cause of infertility.

Investigation of the Husband

This is carried out by the gynaecologist or the andrologist.

- a. History. Personal history including age, occupation, previous marriage and special habits as excessive smoking and alcohol intake. Past history of gonorrhoea, mumps, exposure to X-ray, or previous operation for hernia or varicocele.
- b. General examination, for diseases which depress testicular activity as diabetes mellitus.
- c. Local examination of the genital organs, for abnormalities as hypospadias, undescended testicles and varicocele.
- d. Semen analysis. Semen is obtained by coitus interruptus or by masturbation into a clean sterile container after at least 2-3 days sexual abstinence. A spermicidal free condom can be used. It is examined when it liquefies and this takes about half an hour. The characteristics of normal semen are:
 1. Volume: 2-5 ml.
 2. Reaction: Alkaline (pH 7.2-8).
 3. Sperm count: 60-120,000 per cubic millimeter.
 4. Motility. Within one hour of ejaculation, 25% or more of the spermatozoa should have rapid progressive (forward) motility, or 50% or more should have both rapid and slow progressive motility..
 5. Normal forms 30% or more.
 6. Number of round cells <5 millions/ml.
 7. No pus cells or number <one million/ml.
- e. Testicular biopsy, to show if azoospermia is due to failure of spermatogenesis or due to the presence of bilateral obstruction in the passages between the testes and penis.
- f. Chromosomal study and testing for autoantibodies in husband serum. Done in case of testicular failure. Chromosomal study may show Klinefelter syndrome.
- g. Vasography. Dye is injected to determine the site of obstruction in the vas deferens.
- h. Scrotal ultrasound detects varicocele, small testis, and epididymis anatomy.
- i. Absence of alpha-glucoside oxidase enzyme in semen indicates obstructive azoospermia. It is secreted by the epididymis.

Special Investigations for the Wife

I. Detection of ovulation

A. Symptoms

The following symptoms are suggestive of ovulation:

- (1) Regular cycles are usually ovulatory; (2) the presence of ovulation pain; (3) ovulation discharge (a slight increase in cervical secretion occurs about the time of ovulation); (4) ovulation bleeding which is due to drop in oestrogen level after rupture of the graafian follicle; (5) premenstrual mastalgia; (6) spasmodic dysmenorrhea.

B. Investigations

1. Basal body temperature chart

The body temperature is relatively higher in the second half of the menstrual cycle by 0.2-0.5° C because progesterone elevates the body temperature. The patient is instructed to record her temperature by mouth or per rectum or vagina every morning before getting out of bed (before any activity). She must record the occurrence of any form of infection as sore throat. In a normal ovulatory cycle, the curve is biphasic. In the anovulatory cycle the curve is monophasic.

Note. In a normal ovulatory cycle there is sometimes a drop of temperature about the time of ovulation followed by a rise within 24 hrs and the new higher level is maintained until 24-48 hrs before the next period.

2. Premenstrual endometrial biopsy

One or two strips of endometrium are obtained by a biopsy curette few days before the expected period or on the first day of menstruation. Ovulation is detected by the presence of secretory changes in the endometrium with the characteristic corkscrew glands. The value of this test in infertility: (a) to detect ovulation; (b) it may show a poor secretory endometrium (luteal phase defect); (c) it may reveal tuberculous endometritis.

3. Examination of cervical mucus

A negative fern test in the premenstrual week indicates ovulation. If a drop of cervical mucus is taken during the follicular phase and allowed to dry on a slide, crystals of sodium and potassium chloride will deposit in a characteristic palm-leaf appearance which is seen microscopically. This positive fern test is due to oestrogen. It becomes negative when progesterone predominates. At the time of ovulation the cervical mucus can be stretched into a thread more than 6 cm long without breaking (oestrogen effect). This indicates a positive spinnbarkeit test. If the test becomes negative on day 17 to 21 after being positive on day 12 it denotes ovulation.

4. Vaginal smear

During the luteal phase the smear shows many intermediate cells with folded edges (navicular cells) and many leucocytes (progesterone effect). The smear is taken from the lateral vaginal wall in the premenstrual week and stained, e.g. using Papanicolaou stain. The lateral wall is more responsive to hormonal stimulation.

5. Hormone assays

- a. The estimation of serum progesterone on day 22-24 of the cycle (midluteal phase) can detect ovulation (it has replaced estimation of pregnanediol in urine). Serum level more than 3 ng/ml indicates ovulation. This applies if the cycle is 28 days.

- b. Detection of luteinizing hormone in urine using special home kits (Ovu Quick-Ovu Stick). Ovulation is expected to occur about 36 hours after the midcycle LH surge, but this may not happen. LH can also be measured in saliva.

Failure of ovulation may be temporary and so the above tests may be done on two successive cycles.

6. Ultrasound

Growth of the leading follicle and ovulation can be detected with serial ultrasound. The method is expensive and inconvenient and so reserved for special procedures as In Vitro Fertilization. Ovulation is diagnosed by collapse of the follicle and appearance of fluid in Douglas pouch or the appearance of an early corpus luteum.

7. Direct observation of a fresh corpus luteum by laparoscopy or accidentally during laparotomy is a sure sign of ovulation.

Notes

1. Anovulation is the commonest female cause of primary infertility, while blocked tubes is the commonest female cause of secondary infertility.
2. The mature ovarian follicle usually reaches a diameter of 18-24 mm before ovulation.
3. Spinnbarkeit test is done by pulling mucus from the cervix with mucus forceps, or by placing the mucus on a slide, covering it with a cover slip and then lift the cover slip.
4. Nanogram (ng) is a millimicrogram.

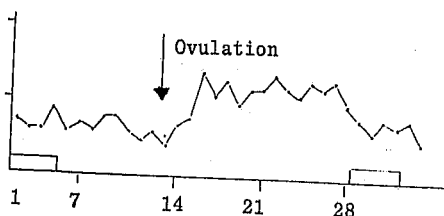


Fig.62. Biphasic basal body temperature curve

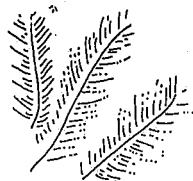


Fig.63. Positive fern test



Fig.64. Vaginal smear in the luteal phase showing many intermediate cells.

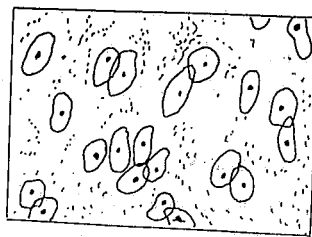


Fig.65. Vaginal smear in the follicular phase showing flat cells with pyknotic nuclei.

II. Investigation of Tubal Patency

1. Hysterosalpingography (HSG)

Patient is placed in the lithotomy position. Bimanual examination is done, then a Cusco speculum is introduced to expose the cervix which is sterilized with antiseptic solution and then grasped with a vulsellum. A radio-opaque substance is injected into the uterus using a special cannula. The procedure is carried out on the x-ray table during the follicular phase of the menstrual cycle, 2-5 days after the end of menstruation. It is done without anaesthesia but the patient may be given an antiprostaglandin half an hour before injection to prevent pain which may also lead to tubal spasm. The medium used is lipiodol (40% iodine in poppy-seed oil). To avoid oil embolism some prefer to use a water-soluble medium as urografin, but this is rapidly absorbed and may not show peritubal adhesions. The amount injected is about 5-10 ml depending upon the size of uterus. Ideally, the amount injected is controlled under the radiological screen (fluoroscopy). An x-ray film is taken immediately after the injection to show the uterus and tubes. Another film is taken after 24 hours if lipiodol is used and after 30 minutes if an aqueous medium is used. If the tubes are patent the second film will show a free peritoneal spill.

Note. Urografin is 40-60% iodine in water.

Advantages

(1) It shows the site of obstruction in the tube and whether it is unilateral or bilateral; (2) diagnose peritubal and pelvic adhesions; (3) diagnose uterine abnormalities as bicornuate uterus, a submucous fibroid or intrauterine adhesions; (4) it has a therapeutic effect because iodine helps absorption of thin adhesions and the dye may displace a mucous plug. Pregnancies have been reported after this procedure.

Contraindications

1. History suggestive of pelvic tuberculosis. HSG can flare up the infection.
2. Pelvic infection in the vagina, cervix or tubes.
3. The presence of tenderness on bimanual examination as this indicates a silent (subclinical) pelvic infection which may flare up after the test.
4. In the presence of menstruation or bleeding from the genital tract to avoid oil embolism.
5. During amenorrhoea as the patient may be pregnant.
6. In the premenstrual period to avoid embolism, endometriosis, false negative result (thick endometrium blocks tubal openings) and disturbance of a possible pregnancy by preventing implantation of a fertilized ovum or causing early abortion..
7. Allergy to iodine.

Complications

1. Pain and shock may occur in sensitive women.
2. Ascending infection as salpingitis and peritonitis, and flaring up of a silent pelvic infection.

3. Oil embolism. Avoided by using a water-soluble medium and not oily preparations, and performing the test 2-5 days after menstruation when the endometrium is least vascular and in absence of bleeding from the genital tract. Also HSG is done under fluoroscopy, so that intravasation is detected early, and the injection is stopped.
4. Oil granuloma in the endometrium or tubes.
5. Endometriosis particularly when the test is done in the premenstrual week when endometrium is thick, so fragments become detached and reach the tube or peritoneal cavity.
6. Cervical lacerations or perforation of uterus by the cannula.
7. Disturbance of a possible pregnancy.
8. Allergic reactions to iodine.

2. Laparoscopy

Laparoscopy is indicated if no cause of infertility is revealed by the routine investigations and if hysterosalpingography is abnormal. A coloured material as methylene blue is injected through the cervix into the uterus to detect the patency of the tubes.

3. Sonohysterosalpingography

Echovist solution or normal saline is injected through the cervix into the uterus. By transvaginal or abdominal ultrasound we see the flow of the fluid in the fallopian tubes and its presence in Douglas pouch indicating tubal patency. The method does not need anaesthesia, and there is no radiation exposure. It also shows uterine anomalies such as fibroids, or septa, and the ovaries are assessed by ultrasound at the same time. Echovist is contraindicated in patients with galactosaemia.

4. Direct Transcervical Cannulation of the Fallopian Tube

We try to pass a catheter through the uterine opening of the tube to perform selective salpingography. This is done using hysteroscopy, transvaginal sonography, fluoroscopy (radiological screening) or blindly. This tubal catheterization is done when proximal tubal obstruction is diagnosed by HSG or laparoscopy, because in about 50% of such cases the obstruction is not organic due to fibrosis but is due to thickened endometrium, tubal spasm, mucous plugs, or plugs made of aggregated histiocytes. It is thus very important to confirm the diagnosis of organic cornual obstruction prior to treatment. In addition organic proximal tubal obstruction should be treated at first by transcervical balloon dilatation before resorting to surgery or In Vitro Fertilization and Embryo Transfer.

Notes

- There is no ideal test to detect tubal patency. False positive tubal obstruction can occur with HSG or laparoscopy. Most gynaecologists use the 2 investigations to complete each other.
- Laparoscopy is the only method which gives a definite diagnosis of peritubal adhesions.
- Echovist is a suspension of galactose microparticles.

III. Investigation of the Uterine Factor

1. Premenstrual endometrial biopsy diagnoses tuberculous endometritis, anovulation, and poor secretory changes due to luteal phase defect.
2. Sonography shows congenital uterine anomalies as bicornuate uterus and the presence of fibroids and intrauterine adhesions (Asherman syndrome).
3. HSG diagnoses congenital anomalies, submucous fibroid and intrauterine adhesions.
4. Hysteroscopy gives the same information given by HSG.

IV. Investigation of Cervical Factor

Postcoital test (Sims-Huhner test). The test must be preceded by semen analysis which showed no abnormality. The test is performed just before ovulation when cervical mucus is excessive and watery and most favourable for the spermatozoa because of the preovulatory oestrogen peak, so it is done on day 12 or 13 of a 28-day cycle. The proper time can be confirmed by the presence of an 18 mm follicle on ultrasound. The couple are told to have a normal intercourse after 2-3 days sexual abstinence and the wife is examined after 2-12 hours. Cervical mucus is collected using a special suction pipette, mucus forceps, or a tuberculin syringe without a needle. The collected mucus is examined for the number of actively motile sperms. The cervical mucus is satisfactory if at least 5 actively motile sperms are seen per high power field.

If the postcoital test is abnormal, it is repeated in the next cycle, after treating any obvious cause as infection, and if still abnormal a sperm penetration test is done to know if the fault is in the cervical mucus or in the sperms.

Notes for the postgraduate

1. Sperm penetration test. It is performed just before ovulation. A drop of cervical mucus is put on a dry slide beside a drop of husband semen. Put a cover slip so that the 2 drops are just in contact with each other and examine microscopically under the high power (Miller-Kurzkrook slide test). The test is normal if sperms are seen penetrating the cervical mucus. If the test is abnormal it is repeated using donated semen from a normal man. If the test becomes normal this means that the fault is in the husband sperms and if the test remains abnormal the defect is in the cervical mucus. Also cervical mucus donated by a normal woman is tested against husband semen. Bovine cervical mucus or egg albumin can be used instead of donor mucus. The test tube can be used instead of the slide test (Kremer test). A graduated capillary tube loaded with cervical mucus is placed into a reservoir of semen. The tube is examined microscopically for the presence of sperms. Examination is done at 30, 60 and 180 minutes.
2. Culture of cervical mucus. Hostile cervical mucus is examined for infection by performing culture and sensitivity test. Chlamydia and Mycoplasma species (*Mycoplasma hominis* and *Ureaplasma urealyticum*) need specific cultures.
3. Immunological tests. If cervical mucus is hostile to spermatozoa, we should test for the presence of antisperm antibodies in the cervical mucus, in the wife serum or in both using the ELISA technique.

V. Investigation of Vaginal Factor

The pH of the vagina is determined by a universal indicator. Excessive vaginal acidity kills the spermatozoa. Also vaginitis has to be excluded.

Note. Causes of poor postcoital test. Wrong timing (commonest cause), oestrogen deficiency leading to scanty thick mucus, cervical infection (destroys endocervical secretory cells, also leucocytes and debris affect sperm migration), increased viscosity of the mucus with Clomid therapy, acidic cervical mucus, destruction of secretory cells following cauterization, presence of antisperm antibodies, dyspareunia and use of lubricants during coitus. Male causes that prevent ejaculation or full penetration of the penis into the vagina as impotence, hypospadias, and premature ejaculation before penetration.

TREATMENT OF INFERTILITY IN THE FEMALE

It is treatment of the cause, for example ovulatory drugs for anovulation, cervical dilatation for stenosed cervix, cauterization for nonspecific chronic cervicitis. Excessive vaginal acidity is treated by an alkaline vaginal douche (one tablespoon of sodium bicarbonate in one litre of water) given 30 minutes before coitus.

Treatment of Blocked Tubes

1. *Tuboplasty*

Tuboplasty gives better results if microsurgical techniques are used. The type of operation depends upon the site of obstruction and may be in the form of salpingolysis (adhesiolysis), salpingostomy, resection and end-to-end anastomosis, or tubouterine anastomosis. However, in proximal tubal obstruction, transcervical balloon dilatation should be tried at first. It is done under fluoroscopy or by using the hysteroscope, ultrasound guide or tactile sensation (blindly). The success rate of tuboplasty ranges widely from 10 to 80%. The best results follow sterilization reversal operations with a success rate about 80% as the tubes are healthy.

Note. In tubouterine anastomosis the occluded part of the tube is excised, and the distal part is anastomosed with the patent interstitial part.

2. *In Vitro Fertilization and Embryo Transfer*

IVF and ET is indicated when tubal obstruction cannot be corrected by surgery and when surgery fails.

Treatment of Hostile Cervical Mucus

1. Cervical infection. Cryocautery for nonspecific chronic cervicitis. It is better than electric cautery or diathermy cautery which may cause excessive fibrosis and cervical stenosis. Chlamydia or mycoplasma infection is treated with tetracycline, erythromycin, or doxycycline.
2. Scanty thick mucus. If associated with anovulation, induction of ovulation will improve the condition. If it is associated with ovulation, we give a small dose of oestrogen as conjugated oestrogens (Premarin) 0.625 mg daily from the 5th to 12th day of the menstrual cycle. The dose can be increased to 1.25 mg daily. If this fails we try gonadotrophins. If this fails we carry out intrauterine insemination, or In Vitro Fertilization and Embryo Transfer (IVF and ET) or Gamete Intrafallopian Transfer (GIFT) to bypass the cervix.

3. The presence of antisperm antibodies. Treatment is by intrauterine insemination to bypass the cervix as the antibodies are in the cervical mucus. If this fails ICSI (intracytoplasmic sperm injection) is performed.

Artificial Insemination

Indications

1. Failure of deposition of semen into the vagina, due to impotence, hypospadias, epispadias, premature and retrograde ejaculation (after prostatectomy), presence of vaginismus, and extreme obesity in either partner.
2. Subfertile semen due to oligospermia, polyspermia, and asthenospermia.
3. Hostile cervical mucus which could not be treated. The technique bypasses the cervix.
4. Severe uterine retroversion.
5. Unexplained infertility.
6. Sterile husband. However, insemination with donated semen is condemned in Moslem countries.

Types

Artificial insemination may be intracervical, intrauterine, intratubal, intraperitoneal, or intrafollicular. Intrauterine insemination (IUI) is the most widely practiced. Whole semen is used for intracervical insemination. Prepared semen is used for other types of insemination. Prepared semen means spermatozoa are prepared by different techniques to obtain the actively motile sperms, and to get rid of prostaglandins and seminal proteins. Prostaglandins lead to uterine cramp and expulsion of the sperms. Seminal proteins may cause anaphylactic reaction.

Technique of Intrauterine Insemination

1. The wife is given clomiphene or gonadotrophins to induce ovulation. This gives better results than when IUI is done without induction of ovulation, and the results with gonadotrophins are better than with clomiphene because of multiple ovulation.
2. Follicular development is monitored with serial ultrasound scanning. When the leading follicle reaches a diameter of 18 mm or more, an injection of human chorionic gonadotrophin, 5000-10000 IU is given IM to induce ovulation. The whole amount of prepared semen (0.3-0.8 ml) is injected, inside the uterine cavity using a special catheter. This is carried out 12 to 34 hours after the injection of HCG. Two IUIs performed 12 and 34 hours after injection of HCG give better results.

IUI is tried for 3-6 cycles. The pregnancy rate is about 25% per cycle of treatment. If IUI fails, in Vitro Fertilization and Embryo Transfer is advised.

ANOVULATION

Occasional anovulation may occur in the normal female. Persistent anovulation is abnormal and leads to infertility. Anovulation may be associated with amenorrhoea, oligomenorrhoea, dysfunctional uterine bleeding or with apparent normal menstruation (anovulatory menstruation).

AETIOLOGY

A. Physiological Causes

Before puberty, the first years after menarche, during pregnancy and lactation, near and after the menopause.

B. Pathological Causes

I. General Causes

(1) Severe anacmia; (2) malnutrition; (3) dieting; (4) obesity; (5) chronic diseases as diabetes mellitus, tuberculosis, chronic liver and renal diseases; (6) drugs as androgens, oestrogens and contraceptive tablets; (7) violent exercise as jogging and training for marathon.

II. Hypothalamic Disorders

Organic lesions, psychological disturbances, anorexia nervosa, gonadotrophin releasing hormone deficiency and Kallmann syndrome, galactorrhoea due to any cause, mental disorders, and functional disturbance of the hypothalamus.

III. Pituitary Disorders

Simmonds disease, Sheehan syndrome, pituitary tumours including prolactinoma, craniopharyngioma and empty sella syndrome.

IV. Thyroid Disease

Hypo-and hyperthyroidism.

V. Adrenal Disease

Hypofunction or Addison disease and hyperfunction – Cushing syndrome and adult-onset adrenal hyperplasia.

VI. Ovarian Causes

The polycystic ovary syndrome, virilizing ovarian tumours, oophoritis due to mumps or typhoid, resistant ovary syndrome and premature ovarian failure leading to premature menopause.

VII. Idiopathic

No cause can be detected in the majority of anovulatory women (80%). It is supposed to be due to functional disturbance of the hypothalamus leading to absence or reduced frequency

of GnRH pulse causing decreased production of FSH and LH. However, we cannot test the hypothalamus to prove this diagnosis.

DIAGNOSIS

1. Basal body temperature. The curve is monophasic.
2. Premenstrual endometrial biopsy. Absence of secretory changes.
3. Examination of cervical mucus. The fern test is positive in the premenstrual week.
4. Vaginal smear taken in the premenstrual week. The cells are flat with pyknotic nuclei (small and dark).
5. Low serum progesterone when tested on 22-24 day of the cycle (<3 ng/ml).

Once anovulation is diagnosed we try to find its cause. A detailed history is taken, clinical examination and laboratory studies are performed to exclude hyperprolactinaemia, hyperandrogenism and thyroid dysfunction. So the hormonal tests performed include:

1. Serum FSH, LH, and prolactin. A high serum level of FSH above 40 mIU/ml indicates ovarian failure. Low FSH (less than 5 mIU/ml) indicates hypothalamic or pituitary problem. An elevated LH:FSH ratio, 2 or more is diagnostic of polycystic ovarian disease (PCO). The commonest cause of hyperprolactinaemia is pituitary adenoma (prolactinoma) which is present in 40-50% of cases.
2. Serum androstenedione, testosterone, and dehydroepiandrosterone sulphate (DHEAS). Androstenedione and testosterone are increased in PCO. Testosterone is also increased in virilizing ovarian tumours. Adrenal tumour increases DHEAS which comes from adrenal gland (almost 100%).
3. Serum 17- α hydroxyprogesterone to exclude adult-onset adrenal hyperplasia.
4. Thyroid function tests including TSH, T3 and T4.

Note. A serum level of FSH above 40 mIU/ml indicates ovarian failure, and a level of 20 to 40 mIU/ml indicates impending ovarian failure.

TREATMENT

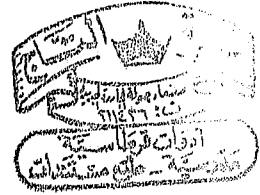
1. General treatment. (a) Proper diet, correction of malnutrition and obese patients are advised to lose weight; (b) treatment of anaemia if present; (c) psychotherapy if necessary.
2. Treatment of the cause, as diabetes and tuberculosis. Anovulation due to hyperprolactinaemia is treated with a dopamine agonist as bromocriptine (Parlodel).
3. Induction of ovulation. Indicated in absence of an organic cause and when the patient desires to conceive. Ovulation is induced by (a) Clomid; (b) Clomid + human chorionic gonadotrophin (HCG); (c) letrozole; (d) gonadotrophins + HCG; (e) gonadotrophin releasing hormone given in a pulsatile manner.
4. Surgical treatment. As removal of a virilizing ovarian tumor and ovarian drilling in the polycystic ovary syndrome.

LUTEAL PHASE DEFECT

LPD is due to decreased production of progesterone from the corpus luteum or early degeneration of the corpus luteum (short luteal phase) or due to inability of the endometrium to respond adequately to a normal hormonal stimulus. The defect can lead to infertility or repeated abortions.

INCIDENCE

About 3-4% of infertile women have inadequate luteal phase.



AETIOLOGY

It includes the following:

1. Reduced follicular maturation is the most common cause. It is due to decreased level of FSH in the early follicular phase or decreased levels of FSH and LH at the time of ovulation.
2. Hyperprolactinaemia. Serum prolactin should be measured in every case of LPD.
3. Hypothyroidism,
4. Hyperandrogenaemia.
5. Deficiency of progesterone receptors in the endometrium so it becomes less responsive to hormonal stimulation. A rare cause.
6. Endometriosis (the ectopic endometrium produces large amounts of prostaglandin F_2 alpha which causes lysis of the corpus luteum and also the occasionally associated hyperprolactinaemia).
7. Athletic women performing violent sports (see general causes of amenorrhoea).
8. Extremes of age. LPD is frequent in the first 3 years after menarche and near the menopause..
9. The first cycle or even 3 cycles after abortion or labour may show LPD.

DIAGNOSIS

1. Premenstrual spotting may be present. Poor function of the corpus luteum leads to irregular ripening of the endometrium and bleeding starts several days before menstruation.
2. Basal body temperature shows a short luteal phase lasting 10 days or less.
3. Midluteal serum progesterone (day 22-day 24) is low (3-10 ng/ml). Level below 3 ng/ml indicates anovulation and above 10 ng/ml indicates normal luteal phase.
4. Premenstrual endometrial biopsy shows a delay of 2 days or more in the development of the endometrium.

TREATMENT

One of the following drugs can be tried:

1. Progesterone or a synthetic progestogen is given in the second half of the menstrual cycle after occurrence of ovulation (started 2 days after the rise in basal body temperature). One progesterone suppository (200 mg) is inserted into the vagina or rectum twice daily till menstruation starts. If the patient becomes pregnant we continue the suppositories for 12 weeks. Oral micronized progesterone can be used.
2. Human chorionic gonadotrophin (HCG) given IM in the second half of the cycle (luteotrophic and prolongs the function of the corpus luteum). Dose is 5000-10000 I.U.
3. Clomiphene to increase FSH level (FSH is necessary for follicular maturation). Treatment of choice.
4. Clomiphene + HCG.
5. Gonadotrophins + HCG. Treatment is costly.
6. Dopamine agonist as bromocriptine in case of hyperprolactinaemia.
7. Corticosteroids in case of increased serum level of DHEAS (dehydroepiandrosterone sulphate) which is derived (almost 100%) from adrenal glands.

Notes

- Nanogram (ng) is a millimicrogram.
- Progesterone should not be started before ovulation as it may block it.
- Natural progesterone is preferred, as synthetic progestogens may not produce adequate secretory endometrium, and may be luteolytic (causing early degeneration of the corpus luteum).

THE LUTEINIZED UNRUPTURED FOLLICLE

The LUF syndrome means failure of the mature graafian follicle to rupture followed by luteinization of its cells with secretion of progesterone. In this way the ovum is not released leading to infertility while the tests for progesterone indicate an ovulatory cycle. Diagnosed by ultrasound. In this case, the graafian follicle will not collapse following the LH peak. However, the diagnosis is often difficult even if ultrasound is performed daily. The LUF syndrome may be associated with endometriosis, or the use of antiprostaglandins, and may occur infrequently in normal menstruating women. Treatment is by induction of ovulation using Clomid or Clomid + HCG or gonadotrophins + HCG. The patient should avoid the use of anti-prostaglandins, as prostaglandins are involved in follicular rupture.

IN VITRO FERTILIZATION AND EMBRYO TRANSFER (IVF and ET)

It means retrieval of oocytes from the ovaries, fertilization in the laboratory, and transcervical transfer of embryos in the uterus.

TECHNIQUE

1. Production of Multiple Mature Ovarian Follicles

This is done by using Clomid and human menopausal gonadotrophins (HMG) in combination or gonadotrophins alone to stimulate the production of multiple mature follicles.

With this regimen premature ovulation may occur leading to cancellation of the cycle before egg retrieval. To avoid this a gonadotrophin releasing hormone analogue (agonist) or an antagonist is given to down-regulate the pituitary gland. The growth of follicles is monitored by repeated estimation of serum oestradiol and pelvic ultrasound. Once the leading follicle has reached a diameter 18 mm or more, an injection of human chorionic gonadotrophin (HCG) is given to induce final maturation of the follicle (5000-10000 IU are given IM). Ovulation generally occurs 36 hours after HCG injection.

2. Aspiration of Eggs (Oocytes)

Aspiration of ova is performed 32-34 hours after the HCG injection. Under ultrasound guidance a needle is passed through the posterior vaginal fornix and directed into the ovary and ova are aspirated. This ovum pick-up is done under general or local paracervical anaesthesia.

3. Fertilization in Vitro

Ova are incubated in a culture medium at 37° C for 4-6 hours for complete maturation then prepared sperms are added for fertilization. When the fertilized egg reaches 8 or 10 cell stage it is transferred to the uterus (this usually takes 36 hours after fertilization).

4. Embryo Transfer

The embryo is placed 2 cm below the uterine fundus using a transcervical catheter without using anaesthesia. Transfer is better done under ultrasound guide to place the embryo in the proper position. This increases the implantation and pregnancy rates. We transfer one or two best quality embryos (Grade I quality) but no more, to reduce the rate of multiple pregnancies with its complications, as abortion and preterm labour. The remaining embryos are frozen, for later use in the same woman. The procedure is repeated for 3-6 successive cycles. Bed rest and sexual intercourse after embryo transfer do not affect the results.

Note. Gonadotrophins include HMG, urinary FSH, and recombinant FSH.

INDICATIONS OF IVF AND ET

1. Absent fallopian tubes either congenitally or secondary to surgery.
2. Tubal obstruction which cannot be corrected by surgery and when surgery fails. IVF is the treatment of choice for cornual obstruction of the tube as it gives better results than reimplantation of the tubes into the uterus.
3. Tuberculous salpingitis and pelvic tuberculosis.
4. Hostile cervical mucus which cannot be treated (we bypass the cervix by intrauterine insemination, IVF or GIFT procedure).
5. Pelvic endometriosis when other lines of treatment fail.
6. Immunological infertility due to the presence of maternal antisperm antibodies and male autoantibodies.
7. Maternal age close to 40 years.

8. Idiopathic infertility.
9. Multifactorial infertility.
10. Ovarian disease. Absent ovaries, streak ovaries, inaccessible ovaries because of pelvic adhesions and failed induction of ovulation. Donated ova and husband semen are used for the procedure. Not accepted in Moslem countries.
11. Absent or diseased uterus in the presence of normal ovaries. The embryo is transferred to a surrogate mother. Not accepted in Moslem countries.

PROGNOSIS OF IVF

The pregnancy rate is 25-30% per treatment cycle. The "take-home baby" rate is up to 60% after 4 cycles of treatment. The prognosis is poor for women over 39 years. Twin pregnancy occurs in about 25%, triplets or more is about 5% of cases. The rate of abortion is about 20% which is not more than the general incidence. However, the rate of abortion is higher in elderly patients, and in those with polycystic ovary syndrome. Ectopic pregnancy occurs in 3% and heterotopic pregnancy in about 1% of cases. The rate of congenital fetal malformations is about 5%, the babies have more neural tube defects, and more oesophageal atresia, but no more cancer in childhood.

Notes for the postgraduate

1. When gonadotrophins are used to stimulate ovulation for IVF, we give a gonadotrophin releasing hormone agonist (analogue) or antagonist to inhibit the secretion of FSH and LH from the pituitary gland. This is known as pituitary down-regulation and has the following advantages: (a) prevention of premature LH surge and premature ovulation. With premature ovulation, no ova can be retrieved, and the treatment cycle is cancelled in about 15% of cases; (b) increase in the number of growing follicles, and so the number of retrieved ova; (c) better quality ova; (d) reduced risk of premature luteinization of follicles (LUF syndrome). The disadvantages of pituitary down-regulation are: (a) more ampoules of gonadotrophins are needed to stimulate the ovaries, and this increases the cost; (b) a higher incidence of ovarian hyperstimulation syndrome; (c) inhibition of LH secretion decreases the production of progesterone from the corpus luteum, and so we need to support the luteal phase. However, the advantages outweigh the disadvantages.
2. Protocols for pituitary down-regulation:
 - a. Long protocol. A long-acting GnRH analogue (e.g. decapeptyl) is given in the midluteal phase, i.e. day 21 of the cycle, then gonadotrophin therapy is started on the second or third day of menstruation. Also, a short-acting analogue can be used in the form of nasal spray (e.g. Suprefact), but it is continued daily till the day before HCG injection.
 - b. Short-acting protocol. A short-acting GnRH analogue is started on day 2 of the menstrual cycle, and gonadotrophin therapy on day 3. The analogue is continued daily till the day before HCG injection.
 - c. Ultrashort protocol. The short-acting analogue is started on day 2 or day 3 of menses and continued for 3 days only, then followed by gonadotrophin therapy.The GnRH antagonists are also used for pituitary down-regulation. They lead to immediate inhibition of FSH and LH secretion without initial flare-up effect.

GAMETE INTRAFALLOPIAN TRANSFER (GIFT)

Oocytes and sperms are placed into the fallopian tube. The procedure is applicable in patients who have normal fallopian tubes.

INDICATIONS

(1) The presence of mechanical block to transcervical embryo transfer; (2) hostile cervical mucus; (3) If IVF fails; (4) pelvic endometriosis; (5) unexplained infertility.

TECHNIQUES

The ovaries are stimulated and ova collected as in IVF. Normally up to 4 ova mixed with prepared husband sperms are injected into the ampulla of the fallopian tube using the laparoscope, i.e. transabdominal GIFT or through the cervix into the isthmic portion of the tube, i.e. transcervical GIFT. Pregnancy rate is about 30%. Ectopic pregnancy occurs in about 5%, it is higher than that with IVF (3%).

ZYGOTE INTRAFALLOPIAN TRANSFER (ZIFT)

The fertilized oocytes in the pronuclear stage (zygotes) are placed into the fallopian tube. It has the same indications as GIFT. In this case the male and female pronuclei are seen in the cytoplasm.

TUBAL EMBRYO TRANSFER (TET)

The embryos (zygotes after cleavage) are placed into the fallopian tube.

INTRACYTOPLASMIC SPERM INJECTION (ICSI)

A single sperm or spermatid is injected into the cytoplasm of the oocyte using a micropipette under the control of the microscope. Fertilization occurs in more than 50% and pregnancy in about 30% of cases or more. In case of obstructive azoospermia, the sperms or spermatids are aspirated from the epididymis and used for injection, i.e. microinsemination after epididymal sperm aspiration (MESA), or sperms or spermatids are obtained by testicular aspiration and used for injection, that is testicular sperm aspiration (TESA). This is done when no sperms are present in the epididymis.

INDICATIONS OF ICSI

1. Male factor infertility. This includes:
 - a. Oligospermia, asthenospermia, and teratospermia. In teratospermia, a single normal sperm is used for injection.
 - b. When the sperms are aspirated from the epididymis or testis.
 - c. Immotile but still alive sperms.
 - d. The presence of antibodies coating the sperms. Antibody laden sperm cannot penetrate the zona pellucida.
2. Previous failed fertilization in IVF.
3. Previous poor fertilization rate in IVF.
4. Limited number of retrieved oocytes.

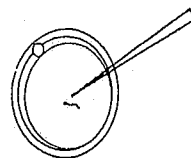


Fig. 65-2.
Intracytoplasmic
sperm injection

5. Refractory unexplained infertility.
6. When pre-implantation diagnosis is needed. ICSI avoids contamination with genetic material of sperms present on the zona pellucida or in the perivitelline space which occurs with IVF.

Notes for the postgraduate

- Eosin-Nigrosin test is used to diagnose immotile live sperms. Under light microscope, dead sperms appear red, as the cell membrane is damaged, and so the cell takes the red eosin stain. Live sperms remain unstained, and appear white, as the cell membrane is intact, and so the cell does not take eosin. The Nigrosin stain provides a background contrast to show the unstained live sperms.
- Causes of yellow semen. Intake of vitamin B, jaundice and long period of sexual abstinence, leading to a high concentration of flavo proteins in the fluid of seminal vesicles.

ASSISTED REPRODUCTIVE TECHNOLOGY (ART)

ART means all techniques which involve retrieval of oocytes from the ovary as well as sperm retrieval and sperm injection.

A. Techniques involving oocyte retrieval

(1) IVF and ET; (2) GIFT; (3) ZIFT; (4) TET.

B. Techniques involving sperm retrieval and sperm injection

(1) ICSI; (2) TESA; (3) MESA.



UNEXPLAINED INFERTILITY

The term is applied when no cause to explain infertility is found and when we fail to establish pregnancy after treating the responsible factor or factors. Infertility is unexplained in about 10% of cases.

AETIOLOGY

Undetected factors may be responsible and include:

1. Abnormal oocyte.
2. Sperm dysfunction. Inability of the sperm to attach to the zona pellucida or to penetrate it.
3. Luteal phase defect (LPD).
4. Luteinized unruptured follicle syndrome.
5. Hyperprolactinaemia. Also, anovulation, and LPD may occur in women with normal prolactin level, due to increased sensitivity to the hormone.
6. Pelvic endometriosis.
7. Minor uterine abnormalities. Minimal intrauterine adhesions may not be detected during hysterosalpingography. For this reason hysteroscopy must be done in all cases of unexplained infertility.

8. Subclinical infection with *Chlamydia trachomatis*, *Mycoplasma hominis* and *Ureaplasma urealyticum*.
9. Subclinical pregnancy losses due to any cause as genetic abnormalities and subclinical hypothyroidism.
10. Immunological disorders. Due to the presence of antisperm antibodies in maternal serum, cervical mucus, paternal serum, or seminal fluid.
11. Psychological disorder leading to anovulation, altered tubal motility, uterotubal spasm, impotence, infrequent intercourse and premature ejaculation.
12. Premature ovarian failure.
13. Female age. Fertility decreases with age, women above the age of 40 show poor response to ovarian stimulation, have aging ova, and the endometrial receptivity is decreased.

DIAGNOSIS

Idiopathic infertility is diagnosed after performing all the following tests:

1. Tests to detect ovulation.
2. Hysterosalpingography. It detects blocked tubes, congenital uterine abnormalities, and abnormal uterine cavity caused by intrauterine adhesions and submucous fibroid.
3. Laparoscopy. It is essential to confirm the presence of blocked tubes, and to exclude peritubal adhesions and pelvic endometriosis.
4. Hysteroscopy.
5. Semen analysis.
6. Postcoital test. If the test is abnormal, it has to be repeated in the next cycle after treating any obvious cause as cervical infection. If still abnormal, a sperm penetration test is done to know if the fault is in the cervical mucus or in the sperms.
7. The pH of the vagina is determined by a universal indicator to exclude excessive vaginal acidity. Also vaginitis has to be excluded.

TREATMENT

1. Drugs

The following drugs are tried empirically:

- a. Clomid.
- b. Dopamine agonists as bromocriptine.
- c. Gonadotrophins + HCG.
- d. Erythromycin, tetracycline or doxycycline for 10 days starting on first day of menstruation. This treats infection with *Chlamydia* and *Mycoplasma* species which could not be detected.

2. Intrauterine insemination (IUI) with prepared semen.

3. Assisted Reproductive Techniques. When 3-6 attempts of IUI fail.

See before.

CONTRACEPTION (FAMILY PLANNING)

INDICATIONS

(1) Limitation of the population; (2) limitation of the family; (3) chronic maternal illness as cardiac or renal disease; (4) previous obstetrical complications as repeated caesarean section; (5) diseases transmissible to the fetus as epilepsy; (6) early years of marriage when adjustment to the new life may be needed; (7) later years of marriage when the family is complete.

METHODS

1. Physiological methods:
 - a. Coitus interruptus.
 - b. Safe period.
 - c. Coitus interfemora.
 - d. Breast-feeding.
2. Mechanical methods:
 - a. The male condom (male sheath or French letter).
 - b. The female condom.
 - c. Vaginal diaphragm (Dutch Cap).
 - d. Cervical cap.
 - e. The vaginal sponge.
 - f. Douching after intercourse.
 - g. Intrauterine contraceptive device (IUCD or IUD).
3. Chemical contraceptives (spermicides).
4. Hormonal contraceptives.
5. Surgical methods (male and female sterilization)

The modern methods of contraception include IUD, hormonal contraceptives and sterilization.

PEARL INDEX (PI)

Raymond Pearl introduced a formula to calculate the pregnancy rate among 100 women using a contraceptive method for one year.

$$PI = \frac{\text{Number of pregnancies} \times 1200 \text{ (number of months used by 100 women in 12 months)}}{\text{Total months of use by all women}}$$

So if 500 women used a contraceptive method for 20 months during which 5 pregnancies occurred, the pregnancy rate is 0.6 per hundred women per year (HWY) calculated as follows:

$$PI = \frac{5 \times 1200}{500 \times 20} = 0.6 \text{ per HWY}$$

Note. Barrier methods of contraception include male condom, female condom, vaginal diaphragm, cervical cap, and vaginal spermicidal agents.

COITUS INTERRUPTUS

The penis is withdrawn just before ejaculation.

Disadvantages

(1) Sexual excitement without satisfaction; (2) neurosis; (3) pelvic congestion syndrome in the female with menorrhagia, increased normal vaginal discharge (leucorrhoea) and backache and prostatic hypertrophy in the male; (4) high failure rate, 18 per hundred women per year (HWY) because the pre-ejaculatory mucus contains spermatozoa.

THE SAFE PERIOD

Normally ovulation occurs 14 ± 2 days before the next period "Rule of Ogino". The spermatozoa remain fertile for about 2 days (24-48 hours) and the ovum survives one day at most (12-24 hours) after release. So if the cycle is 28 days, the fertile period will extend from the 10th to the 17th day, and the rest of the cycle is a safe period.

Disadvantages

(1) Cannot be applied except if the cycles are regular; (2) high failure rate about 24 per HWY because ovulation may occur at any time of the cycle; in fact the safe period is unsafe; (3) coitus is not practiced according to desire but according to rules.

COITUS INTERFEMORA

The male organ is not introduced into the vagina but kept between the thighs.

BREAST-FEEDING

Women are less fertile during lactation as high prolactin level inhibits secretion of gonadotrophins and ovulation. Lactation protects against pregnancy provided (a) lactational amenorrhoea (LAM) is present; (b) regular breast-feeds are given (6-8 feeds per 24 hours including night feeds) and (c) no supplement feeds are given to the infant. This method gives 99% protection during the first 6 months of lactational amenorrhoea. If any of these prerequisites is not fulfilled the lactating mother should receive a contraceptive method, otherwise pregnancy will occur in 5-10% of lactating women.

THE MALE CONDOM

It is made of latex, polyurethane, or rubber. Condoms lubricated with a spermicide as nonoxynol-9 are more effective than condoms without spermicide.

Disadvantages

(1) It interferes with full genital contact so the act is less pleasurable; (2) may interfere with erection; (3) allergic reaction to latex or spermicide may occur in both partners; (4) failure rate is 3-6 per HWY.

Advantages

(1) Technique is simple; (2) avoids sexually transmitted diseases; (3) protects against carcinoma of cervix; (4) medically safe.

Non-Contraceptive Uses of the Male Condom

(1) protection against sexually transmitted diseases; (2) to perform coitus during menstruation; (3) to distend the bladder during cystoscopy to examine a vesicovaginal fistula; (4) to collect semen for semen analysis. The condom must be spermicidal free.

Note. Condoms as thin as 0.02 mm in thickness are now available.

THE FEMALE CONDOM (FEMIDOM)

It is a polyurethane sheath which lines the vagina. It is 15 cm long and 7 cm wide. It has an internal flexible ring at the closed end which covers the cervix and an external ring which remains outside the vagina, and partially covers the vulva. It is for single use only. Failure rate is like that of vaginal diaphragm, 3-6 per HWY.

VAGINAL DIAPHRAGM

It is dome-shaped, made of rubber or latex and with a flexible metal rim. There are different sizes and the number indicates the diameter in millimeters (diameters from 50 to 105, differing by 5 mm). The proper size is known by trying different caps and it must fit well against the vaginal walls all around. A spermicidal cream is placed in the dome of the diaphragm next to the cervix and smeared round the edge. The cap is inserted by the woman before intercourse and is not removed except at least 8 hours after the act so that all the spermatozoa will be killed by vaginal acidity.

Disadvantages

(1) Difficult to apply; (2) cannot be used if there is uterine prolapse, large cystocele, rectocele or retroversion; (3) allergic reaction to latex or spermicide may occur; (4) recurrent cystitis due to compression of the urethra, this forces the bacteria to enter the bladder and causes obstruction to the outflow of urine, also the spermicide promotes the growth of *E. coli* in the vagina, and this predisposes to urinary tract infection; (5) if left in place for long periods it may lead to colonization of *Staphylococcus aureus* and toxic shock syndrome; (6) failure rate is 3-6 per HWY.

CERVICAL CAP

It is cup-shaped, made of rubber and fits directly over the cervix where it is retained by suction and its flexible rim. The caps come in 4 sizes (22, 25, 28, 31 mm). A contraceptive cream must be placed in the cup and smeared around the edge. It can be used if there is prolapse so the Dutch cap cannot be retained. It is difficult to apply and to remove, cannot be applied if the cervix is lacerated and may be displaced during coitus. It is not removed at least

8 hours after coitus. Failure rate is high, 10-20 per HWY due to improper application and displacement during coitus.

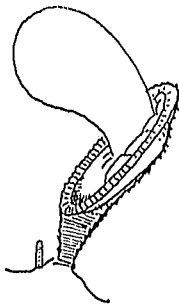


Fig.66. Vaginal diaphragm

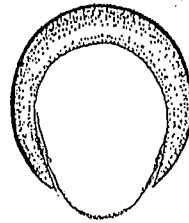


Fig.67. Cervical cap

THE VAGINAL SPONGE

It is a synthetic polyurethane sponge containing one gram of nonoxynol-9 which kills sperms. It also absorbs semen and blocks entrance to cervical canal. It fits into the upper vagina and covers the cervix. It acts both as a mechanical and a chemical contraceptive. It is not removed except at least 8 hours after intercourse. The trade name is "Today".

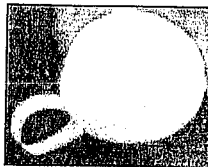


Fig. 67-2. The vaginal sponge

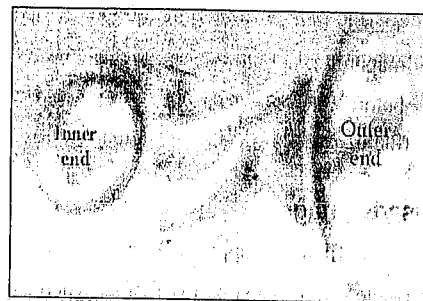


Fig. 67-3. The female condom

DOUCHING AFTER INTERCOURSE

To wash away the sperms before entering the cervix. Fluids used are simple water or spermicidal solution as dilute acetic acid or Coca-Cola which is acidic. Failure rate is high because semen may be ejaculated directly into the cervical canal. It can be used as an emergency method as when the condom breaks.

Note. One litre of plain water to which we add 2 tablespoons of vinegar.

INTRAUTERINE CONTRACEPTIVE DEVICE (IUCD OR IUD)

The IUD is an effective and safe method of contraception. It is used by more than 100 million women worldwide. More than 100 devices have been tried. All devices are made of polyethylene (plastic) which is not irritant to the tissues and is mixed with barium sulphate to be radio-opaque to confirm the presence of the device.

Types

- A. Inert devices made only of polyethylene and are called nonmedicated devices.
- B. Copper devices which release copper.
- C. Hormone-releasing devices which release progesterone or the progestogen levonorgestrel.

Types B and C are called medicated devices.

Inert Devices

The most famous is Lippes loop. It is double S with 2 nylon threads attached to its lower end. The threads protrude through the cervix into the vagina to confirm the presence of the device and facilitate its removal. Lippes loop is available in 4 sizes; A, B, C, and D. Size "A" is the smallest and size "D" is the largest. The size "C" is the standard size which is most commonly used. Size "A" and "B" are suitable for small uteri. Size "D" is used for patients who expel size "C". The action lasts for life (like tooth filling) and the device does not need to be replaced unless complication occurs. However, inert devices have been replaced by medicated devices which have less side effects as pain and bleeding and give better protection against pregnancy.

Copper Devices

The contraceptive effect of the device increases with the increase in its size. So a large device gives a better protection against pregnancy, but leads to more side effects. A small device gives less protection but less side effects. As copper by itself has a contraceptive effect, it allows the use of small devices. Copper devices are the most commonly used at the present time and include the following:

1. Copper T200

This means the surface area of copper is 200 square millimeters. It releases copper at a rate of 15-50 micrograms per day. It protects against pregnancy for 3 years.

2. Copper T220

Surface area of copper is 220 mm^2 . It gives protection for 5 years.

3. Nova T (Novagard)

The surface area of copper is 200 mm^2 . The copper wire contains a silver core. Silver prevents fragmentation of copper and prolongs the life-span of the device which is 5 years.

4. Copper T380 A and Ag

Duration of action is 10 years. Copper T380 Ag has a copper wire which contains a silver core. TCU-380 A is the most effective and most widely used all over the world. It releases copper at a rate of 60-100 $\mu\text{g/day}$.

5. Multiload Copper Devices

Multiload Cu-250 is available in 4 sizes; standard, mini, short, and maxi. Duration of action is 3 years. Multiload Cu-375 acts for 5 years.

6. Copper 7 (Gravigard)

The surface area of copper is 200 mm^2 . It emits copper at a rate of 15-50 $\mu\text{g/day}$. It is active for 3 years. The minigravigard is small to be suitable for small uteri and nulliparas.

Notes

- The inert and old copper devices as Copper T200 and Copper 7 are no longer recommended.
- Copper devices do not increase the serum copper level. Also the minimal daily requirement of the adult woman is 2000-2500 micrograms of copper.
- A copper IUD is available in China which releases a small amount of indomethacin (antiprostaglandin), which reduces the bleeding.
- Data indicate that copper IUD reduces the risk of endometrial carcinoma.
- The copper IUD is not affected by magnetic resonance imaging, so the device need not be removed prior to MRI.

Hormone-Releasing Devices

1. Progestasert

It is a T-shaped plastic device. The vertical limb carries a silastic capsule which contains progesterone (38 mg) which is released at a rate of 65 $\mu\text{g/day}$. Action lasts one year. It is not used in the United Kingdom but still used in the United States. It increases the rate of ectopic pregnancy by decreasing tubal motility.

2. Levonorgestrel T Device (Mirena)

It is a T-shaped plastic device. The silastic reservoir contains levonorgestrel (52 mg) which is released at a rate of 20 $\mu\text{g/day}$. Action lasts for 5 years. It does not increase the rate of ectopic pregnancy. The pregnancy rate is less than 0.2/HWY.

Bleeding and pain are less with hormone-releasing devices as progesterone does not increase the fibrinolytic activity and causes relaxation of the myometrium. Side effects include (a) scanty period and amenorrhoea due to local effect on the endometrium causing atrophy; (b) increased rate of ectopic pregnancy with Progestasert; (c) functional ovarian cysts may occur as well as progestogen side effects as headache, oedema, mood changes, diminished libido and hirsutism. Also the device is costly.

Non-Contraceptive Benefits of Mirena Coil

1. Treatment of dysfunctional menorrhagia.
2. Treatment of endometrial hyperplasia.

3. When combined hormone replacement therapy is indicated in the presence of the uterus to prevent endometrial hyperplasia and endometrial carcinoma.
4. To reduce the size of fibroids and treat associated menorrhagia.

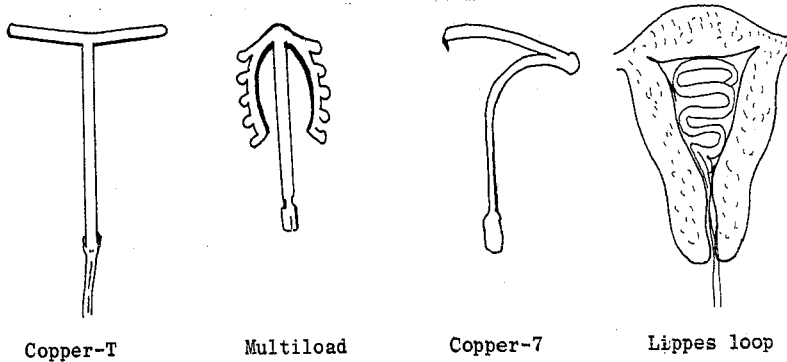


Fig.68. Intrauterine contraceptive devices

Mode of Action

The mode of action of IUD is not definitely known, there are several possibilities, and most probably there is more than one mechanism of action.

1. The device stimulates tubal peristalsis so the ovum reaches the uterine cavity before fertilization or before the endometrium is ready for implantation.
2. It causes utero-tubal spasm preventing meeting of the ovum and spermatozoa.
3. It stimulates uterine contractions, and thus may prevent implantation of the ovum but it does not cause abortion.
4. It makes the endometrium unsuitable for implantation by causing oedema, hyperaemia and leucocyte infiltration in its superficial layer which is in contact with the device.
5. The device attracts macrophages to its site and these phagocytose the spermatozoa or the fertilized ovum. This foreign body reaction is more evident with the copper devices. In addition copper ions inhibit sperm motility and capacitation. Also copper affects glycogen metabolism, synthesis of DNA, and endometrial enzymes as alkaline and acid phosphatase. These enzymes are necessary for the formation of the embryo.
6. Production of prostaglandins. Mild trauma to the endometrium caused by the presence of the IUD may lead to production of prostaglandins which stimulate tubal peristalsis so the ovum reaches the uterine cavity before fertilization, or before the endometrium is ready for implantation. Also stimulation of uterine contractions may prevent implantation of the ovum.
7. Immune mechanism. Some studies showed increased serum levels of immunoglobulins IgG and IgM in women using IUDs. These immunoglobulins may play a role in the action of IUD. This rise could be explained by endometritis or endometrial ulceration with released endometrial fragments which act as antigen.

8. The hormone-releasing device acts by making the endometrium atrophic and unsuitable for implantation, makes the cervical mucus thick, scanty, and viscid thus interfering with ascent of sperm and inhibits sperm capacitation.

Note. IUDs act mainly by preventing fertilization, but can also act by preventing implantation of the fertilized ovum, as when the device is inserted postcoitally.

Side Effects and Complications

1. Pain and shock may occur during insertion due to dilatation of cervical canal and distension of uterine cavity leading to reflex increase in vagal tone. More liable to occur in the nulligravida, women with low pain threshold and when a large device is used. If syncope occurs, 0.6 mg atropine is given I.V.
2. Bleeding. The most common problem. It may be in the form of postinsertion bleeding, menorrhagia, or intermenstrual bleeding. Menorrhagia is frequent in the first 3 months after insertion. Bleeding is less with the hormone-releasing device. The mechanism of menorrhagia is not clear and may be due to increased fibrinolytic activity in the superficial layer of the endometrium which is in contact with the device, or increased production of prostaglandins. The cause of intermenstrual bleeding is explained by mechanical irritation of the endometrium and injury of surface capillaries. Menorrhagia is treated by oral antifibrinolytic agent as Cyklokapron tablets (tranexamic acid) and a prostaglandin inhibitor. Drugs which reduce capillary fragility and increase platelet aggregation as ethamsylate (Dicynone) can be used.
3. Vaginal discharge. Most patients will have a slight watery or mucoid discharge due to mechanical irritation of the endometrium and endocervix. If there is an associated cervical erosion it is unlikely to heal as long as the threads remain in the cervix. Cervical erosions are frequent with copper devices as copper inhibits the growth of the cervical epithelial cells which is necessary for healing of erosion.
4. Pain. The patient may complain of different types of pain as uterine colic, pelvic discomfort, lower abdominal pain, low backache and congestive dysmenorrhoea (due to pelvic congestion). Pain is less with the hormone-releasing device due to the inhibitory effect of the hormone on the myometrium.
5. Pelvic infection. Acute and chronic salpingitis complicate 1-2% of cases. Infection is due to insertion in septic cases, however, the majority of infections result from exacerbation of a latent chronic pelvic infection. Pelvic infection may proceed to tubo-ovarian abscess, pelvic peritonitis, pelvic abscess, general peritonitis and even septicaemia. Frequently the cervical mucus harbours different types of bacteria as streptococci, staphylococci and diphtheroids and these can reach the uterine cavity during insertion of the device. Also organisms including actinomycetes may ascend from the vagina along the tail of the device to reach the uterine cavity. So some gynaecologists recommend removal of the tail of the device to prevent ascending infection. However, this can lead to difficulty when the loop is removed. If infection develops a high vaginal swab is taken for culture and

sensitivity and in severe cases a blood culture is performed. Antibiotic therapy is started and the loop is removed.

6. Perforation of the uterus. It may occur at the time of insertion or later on due to gradual penetration of the uterine wall. The incidence is 0.5 to 2.5 per thousand insertions (average 1 in 1000).

Factors which predispose to perforation include grandmultiparity (uterine wall is thin and fibrous), acute antelexion or retroflexion of the uterus, soft uterus after abortion or labour, presence of a uterine scar as after caesarean section, the skill of the gynaecologist and the mode of insertion. Insertion using the withdrawal technique is safer than the push-out technique. It is safer to insert the loop 6 weeks after abortion or labour and 8 weeks after caesarean section.

Perforation is suspected in the following situations:

- a. Occurrence of severe pain or abnormal bleeding at the time of insertion.
- b. Persistence of pain or bleeding after insertion.
- c. Development of pelvic infection.
- d. Disappearance or shortening of the threads.
- e. Occurrence of pregnancy.

If perforation is suspected and pregnancy is excluded we have to confirm the position of the device by passing a uterine sound to feel the device in the uterine cavity or we do ultrasound scan. If ultrasound is not available, a plain abdominal x-ray is taken. If the device is not seen it means that it has been expelled. If it is seen in the mid or upper abdomen, this indicates that it has perforated the uterus but if seen in the pelvis we cannot be sure that it is inside or outside the uterus. In this case hystero-graphy helps localization. The hysteroscope can be used to visualize the device inside the uterine cavity. In case of perforation the device should be removed as early as possible. Removal is carried out by laparoscopy or laparotomy.

7. Expulsion. Most of the expulsions (50%) occur in the first 3 months after insertion, mostly during menstruation. For this reason the woman is instructed to examine herself periodically and routinely after each period to detect the presence of the threads of the device. The expulsion rate is 2-10% in the first year and falls during the second and third year.
8. Pregnancy. The pregnancy rate is 0.5 to 3 per hundred women in the first year of application and gradually falls in subsequent years. If pregnancy occurs, the device should be removed immediately if the threads are visible to avoid complications in the form of abortion (about 50%), preterm labour (20%) and infection. The rate of abortion is 25% when the loop is removed which is higher than the normal rate of abortion which is 15-20%. Removal should be done immediately before pregnancy advances as the device becomes drawn upward into the uterine cavity. The presence of the loop does not increase the rate of congenital fetal malformation if accidental pregnancy occurs.

9. Ectopic pregnancy. When accidental pregnancy occurs in the presence of IUCD, the risk of being ectopic is increased and reaches 2-3%. The rate of ectopic pregnancy in women not using contraception is 1 in 80 to 1 in 200 average 1 in 100. The device prevents intrauterine but not extrauterine pregnancy. The rate is higher with progesterone-releasing device compared with other types. A history of ectopic pregnancy is a definite contraindication to the use of IUCD.
10. Discomfort to the husband. The husband may complain of the presence of the threads.

Contraindications

1. Suspected pregnancy.
2. When complete protection against pregnancy is essential.
3. Pelvic infection as vaginitis, cervicitis and salpingitis.
4. Uterine malformation as bicornuate uterus.
5. Menorrhagia. IUD increases menstrual flow by 25-50% in many cases.
6. Fibroids causing abnormal bleeding or distorting the uterine cavity.
7. History of ectopic pregnancy.
8. Recent hysterotomy or caesarean section and early puerperium for fear of perforation. It is inserted 6 weeks after abortion or labour and 8 weeks after hysterotomy or caesarean section.
9. Severe anaemia.
10. Severe dysmenorrhoea.
11. Coagulopathy and anticoagulant therapy.
12. Allergy to copper (suspected or proven).
13. Any disorder of copper metabolism, e.g. Wilson disease.
14. Women with suppressed immunity and treatment with corticosteroids for fear of infection.
15. Diabetics for fear of infection.
16. Valvular heart disease. There is a risk of bacterial endocarditis as the organisms may be introduced during insertion or removal of IUD. However, an antibiotic as Ampicillin 2 grams, is taken orally one hour before insertion or removal.
17. The nulligravida. Some do not recommend insertion of loop in the nulligravida as there is a possibility of salpingitis and subsequent infertility, also the insertion is difficult and may be painful.
18. Undiagnosed abnormal uterine bleeding.

Absolute contraindications include: (1) suspected pregnancy; (2) present or recurrent pelvic infection; (3) uterine malformation; (4) fibroids distorting the uterine cavity or causing abnormal bleeding; (5) undiagnosed abnormal uterine bleeding; (6) copper allergy and Wilson disease: for copper devices only.

Technique of Insertion

The loop is inserted immediately after menstruation or on the last day when the cervix is still patulous and to be sure that there is no pregnancy. However, it can be inserted at any time during the menstrual cycle, provided the woman is not pregnant. No anaesthesia is required. The patient is placed in the lithotomy position and examined bimanually to know the size and position of the uterus and to exclude the presence of a contraindication to insertion as bicornuate uterus or the presence of fibroids. A Cusco speculum is inserted to expose the cervix, which is cleaned with antiseptic solution, and then grasped by the vulsellum to steady and straighten the uterus. A uterine sound is passed to determine the length and direction of uterus. There are different techniques for insertion of the IUCD.

- a. The push-out technique. Used for inert devices as Lippes loop. The inserter tip just passes the internal cervical os and the piston then pushes the device inside the uterus. The nylon threads are then cut 3 cm from the cervix.
- b. The withdrawal techniques. Used for copper devices. The inserter is introduced to reach near the fundus of the uterus with the piston fixed below the threaded device, then the outer sheath is withdrawn externally. This technique reduces the incidence of uterine perforation.
- c. The multiloop device is inserted by introducing the inserter inside the uterus to reach the fundus, then the inserter is withdrawn leaving the device in place. No piston is used.

Postinsertion Follow-Up

The patient is examined after the next period to be sure that the loop is in place. Examination is then performed every 6-12 months.

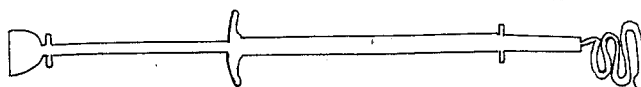


Fig.69. The introducer of Lippes loop

Counselling of the Patient

1. The woman is informed about the type of IUCD to be used, its duration of action, and the date of replacement. She is told that the pregnancy rate is 0.5-3%, and that mild pelvic cramps and mild bleeding may occur for few days after insertion.
2. She is told that menorrhagia is frequent during the first 3 months following insertion.
3. The woman is instructed to examine herself periodically and routinely after each period to feel the threads to be sure that the device is in place.
4. She should report if threads are not felt, if a period is missed, or there is severe pelvic pain and fever to exclude pelvic infection.

Causes of Missing Thread

(1) Expulsion of loop; (2) perforation of uterus; (3) pregnancy; (4) the loop may be displaced upside down; (5) threads cut too short; (6) threads withdrawn inside the cervical canal; (7) detachment of the threads; (8) threads becoming adherent to vagina by thick mucus.

In this case pelvic examination is done and pregnancy is excluded and the device is located as mentioned before using the uterine sound, ultrasound scan, plain abdominal x-ray, hysterosalpingography or hysteroscopy.

Indications for Removal of IUD

(1) When pregnancy is desired; (2) when pregnancy occurs in the presence of the device; (3) when complications occur as bleeding, infection, perforation, etc.; (4) the device has to be kept for a certain period (see before) after which it is removed otherwise the pregnancy rate will be high; (5) menopause, however, we wait one year after the last period before the loop is removed.

CHEMICAL CONTRACEPTIVES (SPERMICIDES)

In the form of vaginal tablets, creams, jellies, foaming tablets, soluble films as C-film, or aerosol foam containing a spermicidal drug as nonoxynol-9. Applied 15-30 minutes before intercourse. They are unreliable, failure rate about 20-25 per HWY and may cause chemical vaginitis or cervicitis, and are messy. The spermicides also promote the growth of E. Coli in the vagina, and this predisposes to urinary tract infection. They are not used alone but with the condom or vaginal diaphragm to improve their efficacy. The C-film is a square water-soluble film applied on the cervix or tip of penis. It dissolves and releases nonoxynol-9.

HORMONAL CONTRACEPTIVES

Mode of Action

Steroidal contraceptives prevent pregnancy by one or more of the following mechanisms:

1. Inhibition of ovulation through inhibition of the midcycle peak of FSH and LH brought about by a direct action on the hypothalamus. Oestrogen inhibits the secretion of FSH and progesterone inhibits LH. The drugs also reduce the ovarian response to pituitary gonadotrophins and interfere with the action of enzymes necessary for the synthesis of the ovarian hormones.
2. Changes occur in the endometrium so it becomes unsuitable for implantation. The drugs cause exhaustion or pseudo-atrophy of the endometrium. The glands become less numerous and the stroma less vascular with diminished production of glycogen by the glands.
3. Contraceptives containing progesterone make the cervical mucus thick, viscid and scanty thus interfering with ascent of spermatozoa.

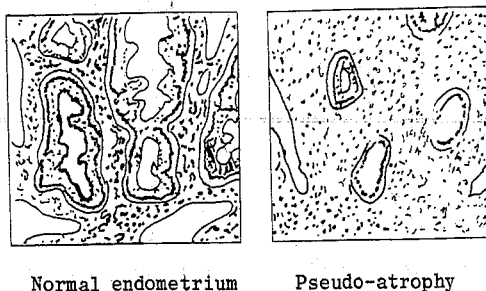


Fig. 70 Endometrium

Types of Hormonal Contraceptives

I. The Combined Oral Contraceptive (COC)

It is a combination of an oestrogen and a progestogen. The oestrogen is ethinyl oestradiol or its derivative ethinyl oestradiol 3-methyl ether (mestranol) which is half the potency of ethinyl oestradiol. The progestogens include several compounds as norethisterone, levonorgestrel and the third-generation progestogens which include gestodene, desogestrel, and noregestimate.

The combined oral contraceptives include 3 types:

- a. Monophasic pills. All the 21 tablets contain the same concentration of oestrogen and progestogen (progestin or progestagen). The original tablets contain 50 micrograms or more of oestrogen and are known as high-dose pills. New preparations contain 20, 30, or 35 micrograms oestrogen (less than 50) to reduce the side effects and are known as low-dose pills.
- b. Biphasic pills. Only one preparation is currently available which is Binovum. The dose of oestrogen is fixed for 21 days but the dose of progestogen is doubled in the last 14 pills.
- c. Triphasic pills. The amounts of oestrogen and progestogen are changed to mimic the hormonal changes of the menstrual cycle. The aim is to reduce the dose of steroids to minimize the side effects. Trinordiol and Trinovum are triphasic tablets. The oestrogen is ethinyl oestradiol and the progestogen is levonorgestrel. The dose of oestrogen is 30 micrograms for 6 days, 40 μg for 5 days, and 30 μg for 10 days. The doses of progestogen for corresponding days are 50 μg , 75 μg , and 125 μg .

Note. A progestogen is any substance which produces secretory changes in the endometrium which has been primed by oestrogen. The third generation progestogens have a weak androgen effect, as they increase the sex-hormone binding globulin thus decreasing the free testosterone.

General Instructions

1. Tablets with low-dose oestrogen (20, 30 or 35 μg) or triphasic tablets are preferred to minimize side effects.

2. The combined tablet is taken daily preferably at night after meals for 21 days starting on any of the first 5 days of the menstrual cycle, preferably on the first day, which is easier to remember, and gives immediate protection against pregnancy. The course is then repeated after one week. Withdrawal bleeding usually starts 2 or 3 days after stopping the tablets.
3. If one pill is missed, a tablet is immediately taken once the woman remembers, and the next tablet is taken at the usual time.
4. If two pills are missed, two pills are taken immediately once the woman remembers, then two tablets are taken at the usual time. It is also advisable to use an additional method of contraception as the male condom for the rest of the cycle.
5. If vomiting occurs within one hour of pill intake, another pill is taken.
6. In absence of breast-feeding COC are started 2-3 weeks after delivery. They are started immediately or within 7 days after abortion.
7. Contraceptive pills can be used for years without a need to stop them periodically.
8. The combined tablet is the most effective contraceptive agent, and provided no tablets are omitted the pregnancy is about 0.1 per HWY.

Note. The value of progestogen in the combined tablet is to increase its contraceptive effect, to prevent endometrial hyperplasia induced by oestrogen, and to regulate the menstrual cycle because oestrogen withdrawal bleeding is prolonged but that due to combined oestrogen and progestogen is like normal menstruation.

Side Effects and Complications of COC

1. **Gastrointestinal tract:**
 - a. Nausea and vomiting may occur due to gastric irritation by oestrogen as well as its effect on the vomiting center. This is frequent in the first 3 months and tend to disappear by time. If persistent use a preparation containing less oestrogen.
 - b. Slight impairment of liver functions may occur.
 - c. COC predisposes to gallstones, cholestatic jaundice, benign and malignant hepatoma.
2. **Central nervous system:**
 - a. Headache and migraine. Headache often occurs during the 7 free days.
 - b. Mood changes as irritability and depression. Depression is a progestin effect. Treated by trying vitamin B6.
3. **Breasts:**
 - a. Breast engorgement, tenderness, and sometimes atrophy.
 - b. Diminished milk secretion in lactating women.
 - c. Galactorrhoea.
 - d. Prolonged use more than 10 years causes slight increase in breast cancer. The relative risk is 1.2. The risk continues for 10 years after stopping the pills. Progestogen-only pills reduce the risk of benign breast lesions as fibrocystic disease of the breast.
4. **Genital tract:**
 - a. Menstrual disorders as hypomenorrhoea, amenorrhoea, (more seen with low oestrogen pills), and breakthrough bleeding. The latter is treated by taking 2 tablets daily until

the bleeding stops, then one tablet daily until the pack is finished. The extra pills should be taken from another pack.

- b. Increased normal vaginal discharge, i.e. leucorrhoea as oestrogen increases the secretion of cervical glands.
- c. Cervical erosion (ectopy) is common.
- d. Oestrogen predisposes to Candida vulvitis and vaginitis.
- e. Increase in the size and red degeneration of uterine myomas. This does not occur with low-dose pills.
- f. Increased risk of cervical adenocarcinoma if taken more than 10 years. A matter of controversy.
- g. Decreased libido which is progestin effect. Some women may have an increased desire probably due to freedom from the fear of pregnancy.

5. Cardiovascular system:

- a. Mild hypertension occurs in about 5% of cases using high-oestrogen tablets for more than 5 years. It is due to water and salt retention, also oestrogen increases the synthesis of renin substrate and angiotensinogen. Low-oestrogen tablets have minimal effects on blood pressure.
- b. Changes may occur in blood coagulation predisposing to venous thrombosis and pulmonary embolism. The high-dose pill increases the risk of arterial thrombosis in women above 40 years, leading to myocardial infarction, and cerebral thrombosis.

6. Metabolic effects:

- a. Increase in body weight due to water and salt retention, and due to anabolic effect of progestogen.
- b. Impairment of glucose tolerance and some women may develop chemical diabetes by antagonising insulin.
- c. Some women may develop folic acid deficiency anaemia.
- d. Oestrogen taken orally elevates the triglycerides (effect on the liver).

7. Skin changes:

- a. Skin pigmentation (chloasma).
- b. Acne vulgaris, hirsutism, and falling of scalp hair as some progestogens have androgenic effects.

8. Allergic Manifestations. As bronchial asthma.

- 9. **Congenital fetal malformations.** Women may continue to take contraceptive tablets unaware that they are pregnant. Recent studies have failed to show any teratogenic effects for the pills. Progestogens taken during the first trimester to treat threatened abortion may cause enlargement of the clitoris and fused labia minora in the female child in 1-2% of cases.

Contraindications to COC

(1) Hypertension; (2) heart disease; (3) acute and chronic liver disease; (4) gallbladder disease and cholestatic jaundice; (5) hyperlipidaemia; (6) family history of breast carcinoma, existing or treated breast cancer; (7) any breast mass; (8) diabetes mellitus; (9) thyrotoxicosis; (10) varicose veins; (11) past history of thrombosis, embolism, cardiovascular or cerebrovascular accident; (12) mental disorders and depression; (13) epilepsy; (14) migraine; (15) allergic diseases as bronchial asthma; (16) oligomenorrhoea and amenorrhoea; (17) glaucoma; (18) optic neuritis and retinal perivasculitis; (19) otosclerosis; (20) fibroids for fear of enlargement and red degeneration. However, the low-oestrogen pill can be used; (21) sickle cell anaemia, leukemia, and polycythaemia; (22) systemic lupus erythematosus; (23) women over 40 years for fear of coronary, cerebral and deep venous thrombosis. However, the low-oestrogen or triphasic pill can be used in women over 40 years and until menopause (age of 50) if there is no risk factor for thrombosis as obesity, hypertension, and diabetes mellitus; (24) smokers over the age of 35 as smoking predisposes to coronary heart disease, and thrombosis; (25) if the patient is receiving a drug which reduces the efficacy of 'COC' as tranquillizers, antihistaminics, and rifampicin used for treatment of tuberculosis; (26) lactating mother; (27) malignant melanoma after its treatment.

The absolute contraindications include:

(1) Liver disease; (2) gallbladder disease and cholestatic jaundice; (3) hyperlipidaemia; (4) existing or treated breast cancer as some tumours are hormone dependent; (5) past history of thrombosis, embolism, cardiovascular or cerebrovascular accident; (6) optic neuritis and retinal perivasculitis; (7) smokers over the age of 35.

Note. Epilepsy is a contraindication. COCs do not increase the fits of epilepsy, but the anticonvulsants reduce the efficacy of the pills. So we use the high-dose pill or another method of contraception.

Drug Interaction

It means one drug interferes with the action of another drug or both drugs combine to produce toxic effects. Certain drugs reduce the efficacy of the combined tablets as sedatives, tranquillizers, anticonvulsants, antihistaminics, antibiotics as ampicillin and rifampicin and mineral oil purgatives. At the same time the pill may reduce the effectiveness of anticoagulants, hypoglycaemic agents, corticosteroids and other drugs.

Relation to Surgery

Postoperative thrombosis is increased in women on COC. The patient should stop the intake of the pill 4 to 6 weeks before major surgery and for the same length of time after surgery.

Beneficial Effects of Combined Oral Contraceptives

1. The combined tablet is the most effective contraceptive agent currently available.

Pregnancy rate is 0.1 per HWY.

2. Combined oral contraceptives are used to treat dysfunctional uterine bleeding, spasmodic dysmenorrhoea, ovulation pain, endometriosis, premenstrual syndrome, and hirsutism. The combined tablet is used to advance or postpone menstruation for social or religious reasons.
3. The use of the combined pill decreases the incidence of benign breast lesions (fibroadenoma and fibrocystic disease of the breast), fibroids, endometriosis, functional ovarian cysts, ovarian carcinoma, endometrial carcinoma, rheumatoid arthritis and pelvic inflammatory disease (the thick cervical mucus caused by the pill interferes with ascent of infection). There is also decreased incidence of anaemia due to decrease in menstrual blood flow, and possible reduction of colorectal cancer. The combined pill also reduces the incidence of ectopic pregnancy by inhibiting ovulation and reduction of PID.

Note. COCs reduce the secretion of gonadotrophins, and so reduce the risk of functional ovarian cysts, i.e., follicular and corpus luteum cysts.

II. The Progestogen-Only Pill (Minipill)

It consists of a small dose of a progestogen as norethisterone or levonorgestrel. It is taken daily without interruption. The tablet should be taken at the same time every day with no more than 3 hours delay as it remains effective for only 27 hours. Available preparations include Microlut (34 tablets), Exluton and Femulen (28 tablets).

Mode of Action

1. Inhibition of ovulation which occurs in about 50% of cases.
2. The pill causes atrophy of the endometrium which becomes unsuitable for implantation.
3. The cervical mucus becomes thick, viscid, and scanty thus interfering with ascent of the spermatozoa (hostile mucus).

Mechanisms 2 and 3 are the main mode of action.

Indications

1. Lactating mother whose fertility is reduced by lactation, and also milk production is not affected.
2. When oestrogen is contraindicated as in case of hypertension, heart disease, diabetes mellitus, history of thrombosis, women over 40 years of age and smokers over 35. The mini pill has no effect on blood pressure or coagulation factors. Also their effect on lipid metabolism and liver is minimal.
3. Women who develop oestrogen side effects while using COC as focal migraine.

The mini pill is less effective than the combined tablet and pregnancy rate is about 3 per HWY as ovulation is not always inhibited (in only 50% of cases).

Contraindications

1. Past history of ectopic pregnancy.
2. Acute mononucleosis.

Side Effects

1. Less effective than the combined tablet.
2. Irregular uterine bleeding, and amenorrhoea are frequent.
3. Headache, nausea, breast tenderness, mood changes, depression, acne, and diminished libido may occur.
4. If pregnancy occurs, the incidence of ectopic pregnancy is increased. The progestogen decreases tubal motility.

Pill Taking

1. Menstruating woman. The pill is started on any of the first 5 days of the menstrual cycle, preferably on the first day which is easier to remember and gives immediate protection against pregnancy.
2. Lactating woman. Six weeks after delivery.
3. Non-lactating woman. At any time during the first 6 weeks after delivery. No need to wait for menstruation to start.
4. Abortion. Immediately or within the first 7 days after abortion.

III. Injectable Contraceptives

1. Progestin-only injectables:
 - a. Depo-Provera (medroxyprogesterone acetate). It is injected IM in a dose of 150 mg every 3 months. Subsequent injections must be given no more than 2 weeks early or 2 weeks late.
 - b. Norstat (norethisterone enanthate). It is injected IM in a dose of 200 mg every 2 months.
2. Combined injectable contraceptives. Composed of both oestrogen and a progestogen. Oestrogen is added to prevent irregular uterine bleeding. Injection is given IM every month (30 ± 3 days).
 - a. Mesigyna. It is a combination of 50 mg norethisterone, and 5 mg oestradiol valerate.
 - b. Cycloprovera and Cyclofeni. It is a combination of 25 mg medroxyprogesterone acetate, and 5 mg oestradiol cypionate. The monthly injectable contraceptive is started within the first 5 days of the menstrual cycle, or at any time if we are sure that the woman is not pregnant. The woman will have regular bleeding 10 to 15 days after each injection due to drop in oestrogen level.

The injectable contraceptive is given deeply into the deltoid muscle (preferred site) or the upper outer quadrant of the gluteus muscle (21-23 gauge needle). The injection site is not massaged to avoid rapid absorption of the drug.

Mode of Action of Injectable Contraceptives

1. Inhibition of ovulation. It is the main action.
2. Effect on cervical mucus, and endometrium. (See above).

Pregnancy rate is about 0.3 per HWY.

Depo-Provera

Indications for Depo-Provera

1. Lactating women as it increases milk secretion.
2. Contraception needed for a short period, e.g. when a woman is immunized against rubella as we need to prevent pregnancy for 3 months, also after vasectomy we need 6-8 weeks for sperm clearance.
3. When oestrogen is contraindicated as in case of hypertension, heart disease, diabetes mellitus, history of thrombosis, women over 40 years and smokers over 35 years.
4. Women who develop oestrogen side effects while using COC as focal migraine.
5. Women who regularly forget the tablet and are unable to tolerate the intrauterine contraceptive device.
6. In patients with sickle cell anaemia as it reduces sickling.
7. In patients with epileptic seizures. Progestins have sedative properties.
8. Mentally retarded women.

Contraindications

1. Nulliparae as return of fertility may be delayed as the drug persists in the body for several months in women who used it for a long time.
2. Acute liver disease and carcinoma of the breast.
3. Women who dislike menstrual irregularities.

Side Effects

1. Menstrual changes in the form of irregular uterine bleeding and amenorrhoea. Amenorrhoea may last for a long time after stopping the injection. Severe bleeding may occur which is very rare.
2. Fertility is delayed about 9 months after stopping the drug.
3. Formation of small follicular cysts in the ovaries which will disappear spontaneously. The ovarian follicles grow and do not rupture as ovulation is inhibited and may form cysts.
4. Weight gain.
5. Headache, nausea, breast tenderness, mood changes, depression, acne, and diminished libido may occur.
6. Osteoporosis may occur due to the hypoestrogenic state, caused by sustained ovarian inhibition.

Non-Contraceptive Uses

Treatment of endometriosis, endometrial hyperplasia, advanced and recurrent endometrial carcinoma, precocious puberty and hirsutism.

Time of Injection of Depo-Provera

1. Menstruating woman. Within the first 7 days of the menstrual cycle, or at any time provided the woman is not pregnant. If given after day 7, a male condom, or a contraceptive vaginal tablet is used for 48 hours (backup method).
2. Lactating woman. Six weeks after delivery.
3. Non-lactating woman. At any time during the first 6 weeks after delivery. No need to wait for menstruation to start.
4. Abortion. Immediately, or with the first 7 days after abortion.

Treatment of continuous or severe bleeding with Depo-Provera

1. Exclude other causes of bleeding from the genital tract.
2. If no cause is found to explain the bleeding, give one combined oral contraceptive tablet daily for 7-21 days, or give 1.25 mg conjugated oestrogens (Premarin) daily for 7-21 days, as the endometrium is atrophic.

IV. Subdermal Contraceptive Implants**1. The Norplant System**

Six silastic capsules containing levonorgestrel are inserted subcutaneously in the inner side of the upper arm in a fan-shaped manner using local anaesthesia. Each capsule contains 36 mg of levonorgestrel which is released at a rate of 80 µg daily (from all capsules) in the first year, then at a rate of 30 µg daily in the next 4 years. Norplant prevents pregnancy for 5 years, then the capsules are removed under local anaesthesia. Pregnancy rate is about 0.5 per HWY. The mode of action and side effects are like Depo-Provera, however, fertility is not delayed after removal of the capsules. The Norplant system has been withdrawn from UK because of the side effects.

2. The Two Rod System (Javelle)

It consists of 2 solid silastic rods. Each rod contains 75 mg levonorgestrel. Pregnancy is prevented for 5 years.

3. Implanon

It consists of one rod which contains 68 mg of etonogestrel which is released at a rate of 40 micrograms daily. It prevents pregnancy for 3 years.

4. Nestrone Implant

It consists of one rod which contains the progestogen nestrone, and prevents pregnancy for 2 years.

5. Uniplant

It is one silastic capsule containing norgestrel acetate, and prevents pregnancy for one year.

All the above capsules and rods are non-biodegradable and are removed once the protective action is finished.

6. Capronor

It is a single biodegradable capsule which releases levonorgestrel and prevents pregnancy for one year.

V. Contraceptive Vaginal Rings

These are silastic rings containing hormones. The ring is inserted by the patient into the vagina. The hormones released are absorbed by lymphatics through the vaginal walls and bypass the liver, so the side effects are less compared with the oral tablets. There are 2 types:

1. The combined vaginal ring. An example is the Nuva ring which releases ethinyl oestradiol and etonogestrel. The ring is inserted into the vagina on the 5th day of the menstrual cycle and left for three weeks, then removed, and reinserted again after one week to allow withdrawal bleeding. It contains hormones to prevent pregnancy for one month. Failure rate is about 0.5 per HWY.
2. The progestogen-only vaginal ring. It releases levonorgestrel. It is replaced every three months. It acts similar to progestogen-only pills. However, failure rate is high.

VI. Contraceptive Skin Patch

The patch contains ethinyl oestradiol and norelgestromin (Ortho Evra). The patch is applied to the skin for one week, then replaced with a new one. Three patches are used for 3 weeks. The fourth week is patch free. Pregnancy rate is 1 per HWY.

VII. Hormone-Releasing Intrauterine Devices

1. Progestasert.
2. Levonorgestrel T device (Mirena). See IUD.

Postcoital Contraception (Emergency Contraception-Interception)

Indications

1. Unprotected sexual intercourse at any time during the menstrual cycle.
2. Rape.
3. Failure of barrier methods, as when the condom ruptures or vaginal diaphragm or cervical cap is displaced.

Methods

1. Hormones

These are given immediately after intercourse or maximally within 72 hours (the morning-after pill). Hormones include:

- a. The combined oestrogen-progestogen tablet. This is known as Yuzpe regimen. If we use a high-dose tablet, 2 tablets are given as mentioned above and repeated after 12 hours. If we use a low-dose tablet, 4 tablets are given and repeated after 12 hours.
- b. The progestogen-only pill. The number of pills depends upon the amount of progestogen in the pill, e.g. if the pill contains 75 micrograms of progestogen (e.g. Ovrette), we give 10 tablets, then 10 tablets after 12 hours. If the pill contains 30 micrograms (e.g., Microlut), we give 25 tablets, then 25 tablets after 12 hours. Postinor pill contains 750 micrograms of levonorgestrel, so one tablet is given within one hour of coitus, and repeated after 12 hours. The minipill is associated with less nausea and vomiting and is more protective compared with the combined pill. With a history of thrombosis, the progestogen-only regimen is preferred.

2. Danazol

600 mg and repeated after 12 hours.

3. Mifepristone

600 mg (12 tablets) are given as a single dose.

4. Mechanical methods

- a. An intrauterine contraceptive device is inserted immediately or up to 5 days after intercourse. It may act by preventing implantation.
- b. Menstrual aspiration is done using a special cannula (Karman cannula) and a 50 ml syringe to aspirate the uterine contents. Procedure is performed one week after intercourse or 1-3 weeks after a missed period.

Mode of Action of the Morning-after Pill

It is not clear, however, it may be through inhibition of ovulation or rendering the endometrium unsuitable for implantation.

Side Effects

Nausea and vomiting may occur. With the combined tablet, nausea occurs in about 50% of cases, and vomiting in about 25%. These complications are less with the minipill being 15% and 3% respectively. An emetic can be taken one hour before the first dose. If vomiting occurs in less than one hour we repeat the dose.

Efficacy

Pregnancy rate with the progestogen-only pill is about 1%; it is 2-3% with the combined tablet and 0.1% with the IUD. Mifepristone prevents pregnancy in nearly 100%. Pregnancy must be excluded if menstruation does not start within 3 weeks following emergency contraception treatment.

Contraception in the Elderly Patient (above 40 years)

Methods

1. The combined oral contraceptives containing low-dose oestrogen (20, 30, 35 μ g). They can be used in women over 40 years and until menopause (the age of 50), if there is no risk factor for thrombosis as obesity, hypertension, and diabetes mellitus. After 50, a barrier method as male condom is used till menopause is established.
2. The triphasic tablets.
3. The progestogen-only pill.
4. Injectable progestogens as Depo-Provera.
5. The subdermal contraceptive implants.
6. Intrauterine contraceptive device.
7. Barrier methods. Male condom, female condom, vaginal diaphragm, cervical cap, and the vaginal sponge.
8. Sterilization.

Postpartum Contraception

Methods

1. Breast-feeding. Lactational amenorrhoea can be used as a method of contraception, provided certain criteria are fulfilled as mentioned before.
2. The progestogen-only pill.
3. Injectable progestogens as Depo-Provera.
4. Subdermal contraceptive implants.
5. Intrauterine contraceptive device.
6. Barrier methods.
7. Postpartum sterilization. It is done on the same day, or at most 2-3 days after delivery, when the uterus is still high in the abdomen. Also bacteria start to appear in the uterine cavity increasing rate of infection. A small incision about 3 cm is made in the anterior abdominal wall at the level of the uterine fundus using general or local anaesthesia. The tubes are picked up and Pomeroy sterilization technique is used.



Progestogen-Only Contraceptive Methods

1. The progestogen-only pill.
2. Injectable progestogens as Depo-Provera.
3. Subdermal contraceptive implants.

4. Progesterone and levonorgestrel releasing intrauterine device.
5. The progestogen-only (levonorgestrel) vaginal ring.

STERILIZATION

- A. Male sterilization by bilateral vasectomy done under local or general anaesthesia. The sperms need 6-8 weeks to disappear completely and 2 negative seminal tests must be obtained after the operation.
- B. Female sterilization by hysterectomy or tubal occlusion. Tubal occlusion may be done by:
 1. **Laparoscopy.** The isthmic parts of the tubes at least 2 cm from the uterine cornua are coagulated with diathermy or clipped (Hulka or Filshie clip) or banded (Falope ring). The method is popular because of small scar, short recovery time, relatively low complications but needs skilled personnel and special equipment. The Hulka and Filshie clip destroy 3 and 4 mm of the tube respectively while the Falope (Yoon) ring destroys a length of 2.5 cm. Clip or ring sterilization fails in about 0.5%.
 2. **Laparotomy.** A small transverse suprapubic incision (3-5 cm in length) can be done (minilaparotomy). Several methods are used to occlude the tube the commonest are fimbriectomy and excision of the middle third of the tube (Pomeroy technique). The failure rate of tubal occlusion is 1-5 per thousand, but it is higher (3 times) when sterilization is done at the time of caesarean section or immediately postpartum. Increased vascularity helps recanalization of the tubes.
 3. **Posterior colpotomy.** An incision is made in the posterior vaginal fornix followed by opening of the peritoneum of Douglas pouch. The tubes are pulled out and occluded as mentioned before.
 4. **Hysteroscopy.** Hysteroscope is used to occlude the uterine openings of the tubes by chemical cautery using silver nitrate or paraldehyde, diathermy cautery, laser, or silicon plug. A silastic device is also placed in the ampullary part of the tube via the uterine end. These methods are still experimental.

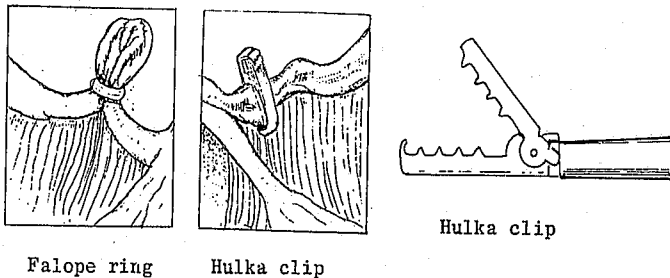


Fig.71. Tubal Occlusion

CHOICE OF THE CONTRACEPTIVE METHOD

The ideal contraceptive method should be 100% effective, easy to use, completely reversible and does not delay return of fertility; totally acceptable, absolutely free of side effects, inexpensive and widely available. No such method exists.

1. The combined contraceptive pill is the most reliable method.
2. For the newly married couple advise the pill or the condom.
3. For the multipara advise the pill or IUD or a barrier method (condom or vaginal diaphragm).
4. For the lactating woman the best is IUD or a barrier method. The mini-pill or Depo-Provera or contraceptive implants as Norplant can be prescribed.
5. Sterilization may be considered in some cases.

Note for the postgraduate

Methods for tubal sterilization (occlusion-ligation) at laparotomy:

1. Pomeroy method. The tube is grasped in its mid-portion with a small atraumatic clamp such as Babcock clamp, and a loop of the tube is elevated. The base of the loop is ligated with No. 1 plain catgut. The loop is excised with scissors. Plain catgut is preferred to keep the tubal stumps away from each other as it is rapidly absorbed.
2. Fimbriectomy (Kroener method). The fimbriated end of the tube is excised.
3. Irving method. The isthmic part of the tube is divided. The stumps are ligated. A small incision is made on the posterior uterine wall near the cornu. The muscle wall is penetrated with a mosquito clamp for a distance of 2 cm to make a pocket. The proximal tubal stump is buried into the pocket. The distal tubal stump is buried between the two leaves of the broad ligament.
4. Uchida method. The mid-portion of the tube is grasped. A 1:1000 epinephrine in saline solution is injected subserosally, creating a bleb over the tube that is then incised. The tube is then divided between two haemostats. The serosa over the proximal tubal segment is bluntly dissected towards the uterus, exposing about 5 cm of the tube which is resected. The proximal stump is then covered with serosa. The mesosalpinx is closed leaving the distal stump open to the peritoneal cavity. Fimbriectomy can be added to the procedure to enhance effectiveness.

Total salpingectomy and Madlener method are now abandoned because of the high failure rate. In Madlener technique a loop of the tube is ligated and crushed, but without excision.

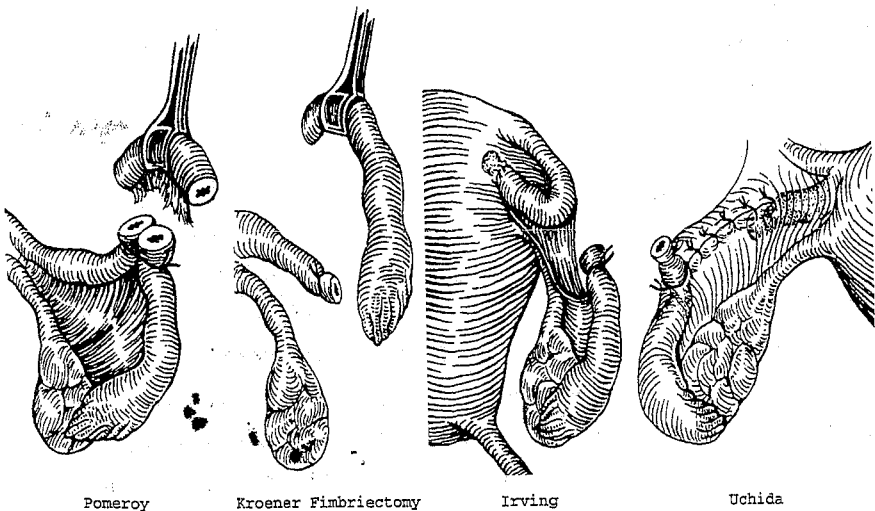


Fig. 71-2. Sterilization at laparotomy

SECTION VIII

DISEASES AND SWELLINGS OF THE VULVA

ULCERS OF THE VULVA

AETIOLOGY

1. Traumatic Ulcer

Due to defloration injury or infected perineal tear or episiotomy.

2. Inflammatory Ulcers

A. Sexually Transmitted Diseases

- Syphilitic ulcers. (a) Chancre, usually single, rounded with a sharp edge, painless unless secondary infected; (b) ulcer due to breaking down of condylomata lata; (c) ulcerating gumma which is surrounded by oedema and induration.
- Soft sore (chancroid).
- Granuloma venereum.
- Lymphogranuloma venereum.
- Herpetic ulcers due to genital herpes.

B. Non-Sexually Transmitted Diseases

- Tuberculous ulcers. Single or multiple with a serpiginous outline, undermined edge and yellow floor.
- Bilharzial ulcers. Usually multiple, superficial with a granular floor.
- Diphtheritic ulcer. Occurs in children, covered by a greyish membrane which bleeds on removal.
- Ulcers associated with Crohn's disease. They look like knife cuts in the skin.
- Ulcers associated with lichen planus.

3. Neoplastic Ulcers

- A. Basal cell carcinoma (rodent ulcer).
- B. Squamous cell carcinoma.

4. Aphthous Ulcers

As in the mouth, these ulcers may occur from time to time in the vulva, lower vagina and anus. They are painful shallow ulcers with a yellow base and bright red margin. Sometimes they are cyclical appearing in the premenstrual phase, and healing during and after menstruation. They are most often located on the labia minora. Healing occurs within a week without scarring.

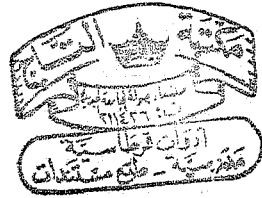
5. Vaccination Ulcer.

6. Behçet Syndrome

It is characterized by recurrent cyclical ulceration of the mouth and vulva, eye lesions as conjunctivitis and iridocyclitis, skin nodules, joint pains and sometimes degenerative lesions in the central nervous system. The aetiology of the ulcers and syndrome is not known. Allergy, autoimmunity, vitamin deficiency, psychological and genetic factors have been suggested but not definitely proved. Treatment by corticosteroids and antibiotics if there is secondary infection but the result is unsatisfactory.

PRURITUS VULVAE

It is the desire to scratch the vulval area.



AETIOLOGY

A. General Causes

(1) Diabetes mellitus; (2) liver disease as biliary cirrhosis, jaundice and hepatitis C; (3) chronic renal disease; (4) lymphoma and leukemia; (5) allergy to foods, drugs or clothes as synthetic underwear; (6) deficiency of vitamin A, B2, B12, folic acid and iron. Hypochromic and macrocytic anaemia may cause vulval itching; (7) achlorhydria (which is an autoimmune disease); (8) hyperthyroidism and hypothyroidism, due to dry skin; (9) menopause (senile pruritus) due to diminished blood supply and atrophy of the skin; (10) psychological disturbances, the scratch habit is easily developed.

Note. The cause of pruritus in liver disease is increased bile salts, however, the cause is unknown in hepatitis C. In chronic renal disease it is due to elevated plasma histamine.

B. Local Causes (90% of cases)

(1) All types of vulvitis; (2) irritating vaginal discharge as in case of trichomonas or candidal infection, 80% of cases of vulval pruritus are associated with vaginal discharge; (3) skin diseases as eczema; (4) parasitic infestation as pediculosis and oxyuris; (5) chronic vulval dystrophies; (6) carcinoma in situ and invasive carcinoma; (7) urticaria; (8) insect bites; (9) pelvic congestion as in coitus interruptus.

C. Idiopathic

No cause can be discovered.

DIAGNOSIS

History

Ask about the points mentioned under the aetiology. It is necessary to know if other areas of the body are affected because the vulval lesion may be one part of a widespread skin problem.

Physical Examination. General, abdominal and local.

Investigations

The following tests may be done according to the clinical findings: (1) urinalysis (for sugar); (2) stool analysis (oxyuris); (3) complete blood count (anaemia and leukemia); (4) serum iron, folate and B12; (5) glucose tolerance test; (6) liver function tests; (7) kidney function tests; (8) thyroid function tests; (9) fractional test meal for achlorhydria; (10) bacteriological examination of vaginal discharge; (11) examination of scrapings from vulval skin for fungus infection; (12) colposcopic examination of the vulva; (13) biopsy from suspected lesions; (14) skin sensitivity tests.

TREATMENT

1. Treatment of the cause as control of diabetes mellitus and *Candida* infection.
2. General treatment: (a) Sedatives as phenobarbitone especially at night to prevent scratching; (b) antihistaminics; (c) oestrogens by mouth or locally in menopausal patients; (d) cotton underwear.
3. Local treatment: (a) Local cleanliness. The vulva is washed several times daily with 1% sodium bicarbonate solution (soothing agent); (b) antipruritic agents as hydrocortisone, antihistaminic and anesthetic ointment.
4. Treatment of resistant cases: (a) Exposure of the vulva to ultraviolet rays. This may act by treating undiagnosed fungus infection; (b) intradermal injection of triamcinolone may be used. If this fails we try subcutaneous injection of absolute alcohol (90%). Few drops (0.1-0.2 ml) are injected subcutaneously at 1 cm apart; (c) division of all cutaneous nerves by a circular incision around the vulva (Ball's operation). It has been used in some refractory cases with good results.

CHRONIC VULVAL DYSTROPHIES

Dystrophy means poor nutrition. The term is applied to describe lesions characterized by hyperkeratosis (thickening of the horny layer) and abnormal thickening or thinning of the epithelium (Malpighian layer) with chronic inflammatory reaction in the subepithelial connective tissue (dermis).

Vulval dystrophies are classified as:

1. Hyperplastic dystrophy with atypia or without atypia.
2. Atrophic dystrophy or lichen sclerosus.
3. Mixed dystrophy. The lesion consists of hypoplastic and hyperplastic areas with or without atypia.

The areas affected include vulval skin, perineum, perianal area and skin of inner sides of the thighs.

In the past the hyperplastic dystrophy was termed leucoplakia and lichen sclerosus was termed kraurosis vulvae.

Note. Atypia or dysplasia or abnormal hyperplasia means the cells show abnormal nuclear changes.

HYPERPLASTIC DYSTROPHY

The vulva shows well defined raised white patches due to hyperkeratosis. If the hyperkeratosis is slight the affected areas appear red. Fissures and ulcers may appear due to scratching. Microscopically there is hyperkeratosis, the epithelium is thick with overgrowth of the papillae (rete pegs). The epithelial cells may or may not show abnormal activity (with or without atypia). The subepithelial connective tissue shows chronic inflammatory cells (lymphocytes and plasma cells).

LICHEN SCLEROSUS

This is the atrophic form of dystrophy. The skin of the vulva becomes thin, atrophic (like cigarette paper) dry, smooth and white in colour. There is marked decrease in the subcutaneous fat. Atrophy may lead to disappearance of the clitoris, labia minora and narrowing of the vagina. Microscopically there is hyperkeratosis and marked thinning and atrophy of the epithelium with disappearance of the papillae. The subepithelial connective tissue is fibrosed and infiltrated with chronic inflammatory cells. It is the most common white lesion of the vulva.

Aetiology

The cause of chronic vulval dystrophies is unknown. Predisposing factors may include chronic mechanical irritation, allergy, autoimmunity, achlorhydria which is an autoimmune disease, metabolic disturbances as diabetes mellitus, fungus infection, deficiency of vitamin A, B2, B12, folic acid and iron, and psychoneurosis (the scratch habit is easily developed and leads to mechanical irritation). Chalone may play a role. These are tissue proteins secreted by the epidermis. They inhibit mitotic activity. Increased action leads to epithelial atrophy and decreased action leads to hyperplastic changes. Action of chalone may be affected by hormones and other agents.

Symptoms

The disease is mainly seen in postmenopausal women. The condition may be symptomless, however, the main complaint is pruritus. Pruritus tends to be severe with hyperplastic dystrophy and mild with lichen sclerosis. Scratching may lead to ulceration, secondary infection and local pain. Dyspareunia from narrowing of the vagina.

Diagnosis

Biopsy is essential for diagnosis and to diagnose cases with atypia and to exclude other lesions as carcinoma in situ. Multiple toluidine blue or colposcopic directed biopsies should be taken because the histological appearance may vary in the different sites of the lesion. At the same time, we try to find a predisposing factor as diabetes mellitus, fungus infection ... etc.

Differential Diagnosis

White lesions of the vulva may be due to: (1) vulval dystrophies; (2) carcinoma in situ; (3) Paget disease; (4) invasive carcinoma; (5) candidiasis; (6) condyloma acuminatum; (7) condyloma latum; (8) leucoderma; (9) psoriasis; (10) lichen planus; (11) intertrigo; (12) avitaminosis A; (13) vitiligo.

Treatment

1. Specific Treatment

Hyperplastic dystrophy without atypia is treated by local corticosteroids which relieve pruritus and also lead to dermal atrophy (1% hydrocortisone cream applied 3 times daily for 6 weeks). Hyperplastic lesion with atypia is treated by surgical excision for fear of malignancy. Laser can be used for local excision. Lichen sclerosus is treated by testosterone cream 2% (applied 3 times daily for 6 weeks then a maintenance course of once daily or once every other day is continued indefinitely). Topical testosterone results in dermal hypertrophy. Patient is informed about the possible masculinizing side effects. In mixed dystrophy corticosteroid cream is applied for 6 weeks followed by testosterone cream as mentioned before.

2. General Treatment

Treatment of any predisposing factor as candidiasis and diabetes mellitus. The underwear should be of cotton. Avoidance of perfumes, deodorants, synthetic fabrics and pantyhose which prevent evaporation of sweat.

SWELLINGS OF THE VULVA

AETIOLOGY

1. Congenital abnormalities. Hypertrophy of the clitoris. Hypertrophy of one or both labia minora. Congenital dermoid cyst which occurs only in the midline. Accessory nipple or breast (the breasts and vulva lie in the milk line which extends from the axilla to the vulva).
2. Traumatic lesion. Haematoma.
3. Inflammatory conditions. Acute vulvitis, furuncle, carbuncle, condylomata acuminata, syphilitic lesions (condylomata lata and gumma), hypertrophic tuberculosis and bilharzial papillomata.
4. Neoplastic swellings. Benign and malignant tumours (primary and secondary).
5. Swellings due to vascular changes. Varicose veins, oedema, elephantiasis and pseudo-elephantiasis.
6. Swellings of Bartholin gland. Bartholinitis, abscess, cyst, adenoma and carcinoma.
7. Urethral conditions. Caruncle, carcinoma, prolapse of the urethral mucosa, diverticulum of the urethra and cyst of Skene tubules.

8. Retention cysts. Sebaceous cyst, dermoid cyst, hymeneal and clitoridal cyst, hydrocele of the canal of Nuck and endometrioma.
9. Other swellings. Inguinal hernia and the testicles may be found in the labia majora in case of androgen insensitivity (testicular feminization syndrome).
10. Swellings may appear at the vulva but are not true vulval swellings as vaginal and uterine prolapse, inverted uterus, vaginal, cervical and uterine tumours projecting through the vagina.

Many of the above lesions are described elsewhere; this chapter is concerned only with those which are not.

HAEMATOMA OF THE VULVA

Aetiology

It may occur after direct trauma, surgical trauma as removal of Bartholin cyst, obstetric trauma as instrumental deliveries, poor haemostasis during repair of episiotomy or perineal tear and rupture of varicose vein during labour.

Clinical Picture

It appears as a tender bluish swelling. At first the consistency is cystic then becomes firm when blood coagulates.

Treatment

If the haematoma is small we wait for spontaneous absorption but if it is large or increasing in size, it is incised, blood evacuated, bleeding vessels ligated and the cavity is obliterated. Infected haematoma is treated like an abscess by incision and drainage.

CONDYLOMATA ACUMINATA

See sexually transmitted diseases.

OEDEMA OF THE VULVA

Aetiology

(1) General causes of oedema as heart and renal failure and nutritional oedema; (2) pressure from pelvic tumours; (3) vulval infection; (4) angioneurotic oedema; (5) pre-eclampsia and obstructed labour.

Treatment

The treatment is that of the cause. Symptomatic relief by resting the patient in bed the foot of which is elevated. Vulval oedema associated with a pelvic tumour indicates that the tumour is nearly always malignant.

ELEPHANTIASIS OF THE VULVA

Aetiology

It is secondary to chronic lymphatic obstruction leading to lymphatic oedema which stimulates proliferation of the subcutaneous connective tissue. Lymphatic obstruction may be congenital or acquired as in case of filariasis (*Wuchereria bancrofti* worm) and chronic infections which heal by fibrosis like lymphogranuloma venereum, granuloma venereum and tuberculosis. Occasionally the cause is obscure. Pseudo-elephantiasis results from the presence of multiple bilharzial papillomata.

Clinical Picture

There is hypertrophy and oedema of the labia majora and minora. The skin becomes thickened, indurated and hyperkeratotic and resembles that of the elephant.

Treatment

It is treatment of the cause and excision of the affected tissue.

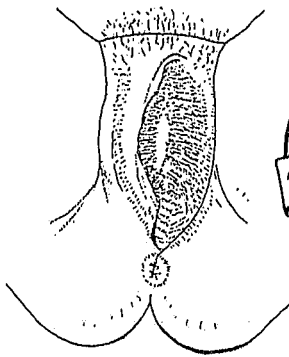


Fig.72. Haematoma of the vulva

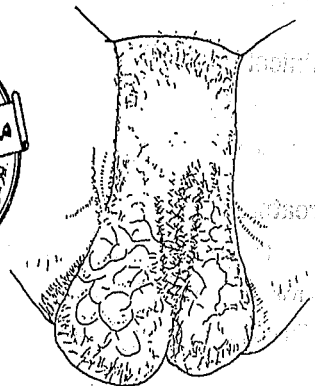


Fig.73. Elephantiasis of the vulva

BARTHOLIN CYST

Types

It is the most common cyst of the vulva. There are 2 types, cyst of the duct which is common and cyst of the gland which is rare because the gland lies between the superficial and deep perineal membranes and so it is difficult for the gland to distend. The cyst of the duct is lined by transitional or squamous epithelium and the cyst of the gland is lined by columnar or cuboidal epithelium.

Aetiology

The cyst is due to obstruction of the main duct or the opening of an acinus by fibrosis. This fibrosis follows infection or trauma as

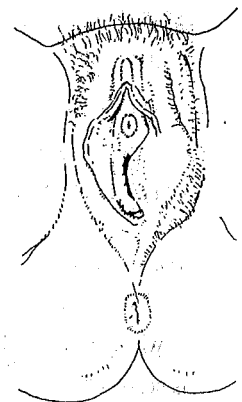


Fig.74. Bartholin cyst

repeated friction during cycling and mediolateral episiotomy. The infecting organism may be the *Gonococcus*, *Chlamydia*, *Staphylococcus*, *Streptococcus*, *E. coli*, *Trichomonas vaginalis* as well as any other pyogenic organism. Another possible factor causing obstruction of the duct is the presence of thickened or inspissated mucus near the ductal opening. This mechanism can explain spontaneous disappearance of a cyst after sudden outflow of mucus.

Clinical Picture

The cyst contains mucus. It forms an oval cystic swelling in the posterior part of the labium major. The swelling is painless unless infected.

Treatment

It is by excision or marsupialization which means incision of the cyst and suturing its edges to the surrounding skin. It is easy with less bleeding, preserves the lubricating function of the gland and the convalescence is short and is the treatment of choice. However, surgical excision is indicated in the postmenopausal woman because there is a possibility of a malignant lesion involving the Bartholin gland at this age. Excision is also done if the cyst is recurrent.

ACUTE BARTHOLINITIS

The infecting organism as mentioned above. The patient complains of local pain and dyspareunia. On examination the covering skin is red, warm and may be oedematous. The gland is felt enlarged, indurated, and tender. The orifice of the duct may be seen as a small red spot. When the gland is compressed between the index finger and thumb, a drop of pus may exude from the orifice. This may be examined by Gram stained film, culture and sensitivity test. The end result of acute bartholinitis is complete resolution under treatment, abscess formation, or chronic bartholinitis. In the latter case the gland is felt as a tender nodule. Treatment of acute bartholinitis is by rest in bed, antibiotics, hot fomentation, and sitz baths.

BARTHOLIN ABSCESS

In most cases, the Bartholin abscess develops as a result of infection of the fluid content of Bartholin cyst. The route of entry of organisms is not yet determined but probably through the stenosed opening of the Bartholin duct. However, the aspirated fluid from a cyst or abscess may be sterile. The treatment of Bartholin abscess is incision and drainage or marsupialization.

URETHRAL CARUNCLE

It is a small fleshy tumour few millimeters in diameter and rarely exceeds 1 cm. It arises from the floor of the urethra and protrudes from the external meatus. It is bright red in colour, sessile or pedunculated and may be very tender. It occurs only in the female urethra particularly in postmenopausal women. It is almost invariably single.

Pathology

The caruncle is made of 3 elements, a covering epithelium which is transitional epithelium, granulation tissue infiltrated with lymphocytes and plasma cells and blood vessels. So there are 3 pathological types: (1) papillomatous caruncle which is papilloma of the urethra (true caruncle); (2) granulomatous caruncle which consists mainly of granulation tissue. It results from chronic urethritis and in most cases it is due to *Trichomonas* infection; (3) angiomatous caruncle which contains many dilated blood spaces.

Symptoms

The condition may be symptomless, however, the patient may complain of one or more of the following: local pain, dysuria, dyspareunia, bleeding particularly during urination or intercourse and the presence of a swelling.

Differential Diagnosis

Carcinoma of the urethra and prolapse of the urethral mucous membrane.

Treatment

Wedge excision of the area from which the caruncle arises because it is liable to recur. The site should then be cauterized with diathermy. In case of chronic urethritis, the associated infection is treated.

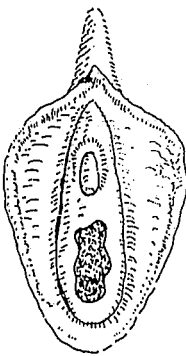


Fig.75. Urethral caruncle

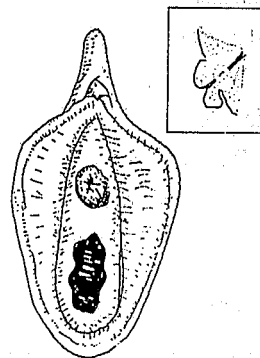


Fig.76. Prolapse of the urethral mucosa

PROLAPSE OF THE URETHRAL MUCOSA

This may be acute or chronic.

Acute Type

Almost all cases occur in premenarcheal and postmenopausal women suggesting a relationship to oestrogen deficiency. It may suddenly appear after coughing, crying or severe straining. It forms a purple tumour of variable size with the urethral meatus at its center because the whole circumference of the lower urethral mucosa prolapses. This helps to

differentiate it from urethral caruncle and carcinoma. The patient complains of pain, dysuria and sometimes reflex retention of urine. After few days the prolapsed tissue ulcerates and may bleed due to strangulation.

Treatment

Hot sitz baths to reduce congestion followed by manual reduction of the prolapse under anaesthesia with insertion of a Foley catheter for several days or surgical excision of the redundant mucosa. A third line of treatment is simple ligation of the prolapsed mucosa over a Foley catheter to cause sloughing away of the prolapsed mass. However, surgical excision is the best treatment.

Chronic Type

It is common in old age when atrophy causes the external meatus to gape and allows some part of the urethral mucosa – usually the posterior rim – to project as a small tumour. The condition is asymptomatic unless the exposed tissue becomes infected when frequency and dysuria are likely. No treatment is required unless symptoms are present. In this case the prolapsed mass is excised.

DIVERTICULUM OF THE URETHRA

This may be a congenital abnormality or may follow the rupture of a paraurethral abscess into the urethra. It forms a swelling on any aspect of the urethra but most often on the posterior or posterolateral aspect. A posterior diverticulum projects into the vagina and may appear at the introitus. Pressure on the swelling may lead to escape of pus or urine from the urethral meatus. However, in most cases the opening into the urethra is often valve like and no material can be expressed. The opening of the diverticulum can be seen through the urethroscope. The condition has to be distinguished from urethrocele, cyst of Gartner duct or Skene tubules. Treatment is by excision with closure of the small urethral defect. Histological examination of the excised tissue must be done as carcinoma can develop in a diverticulum though it is rare.

CYST OF SKENE (PARAURETHRAL) TUBULES

Infection blocking the opening of the tubule will lead to cyst formation. It forms a small swelling on the lower part of the anterior vaginal wall rather than on the vulva. The cyst can become infected leading to a paraurethral abscess. The Skene tubules arise as outgrowths of the urogenital sinus. In the male they form the prostate.

EPIDERMIOID CYST, IMPLANTATION DERMOID

Due to implantation of epithelial cells of the skin below the surface during repair of a perineal tear or episiotomy or as a result of circumcision with removal of the clitoris. The lining stratified squamous epithelium secretes sebaceous material forming a cyst. When congenital it is always in the midline. Treated by excision. These cysts cannot develop from implants of vaginal epithelium which does not secrete sebum.

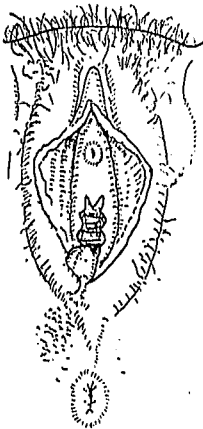


Fig.77. Implantation dermoid

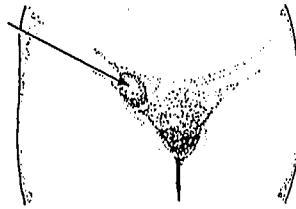


Fig.78. Hydrocele of the canal of Nuck

SEBACEOUS CYSTS

Sebaceous and apocrine glands are present in the mons veneris, labia majora and minora. Obstruction of the gland duct by debris or fibrosis leads to cyst formation. These cysts are small, often multiple and characterized by the presence of a punctum. Treated by excision or incision and drainage if infected.

HYDROCELE OF THE CANAL OF NUCK

Serous fluid collects in the pouch of peritoneum found in the inguinal canal and accompanies the round ligament. It is normally obliterated in the female. In the male this pouch is called the processus vaginalis. It forms an elongated cystic swelling in the inguinal canal and upper part of the labium major. Sometimes the cyst is communicating with the peritoneal cavity and so can be emptied on pressure and disappears when the patient lies down. Treated by excision and dealing with any inguinal hernia.

ENDOMETRIOMA OF THE VULVA

The lesion appears as a small dark blue cyst which increases in size and becomes tender during menstruation. It is lined by endometrium and contains altered blood. There is usually a history of surgical or obstetrical trauma as evacuation. The lesion may also occur in the labium major near the insertion of the round ligament.

HYMENEAL AND CLITORIDAL CYSTS

These arise from the lower part of the Gartner (Wolffian) duct and are lined by cubical epithelium. They may become infected leading to recurrent abscesses.

Note: Cystic swellings of the vulva include: (1) haematoma; (2) Bartholin cyst (the commonest); (3) sebaceous cyst; (4) epidermoid cyst; (5) hydrocele of the canal of Nuck; (6) endometrioma; (7) cyst of Skene tubules; (8) hymenal and clitoridal cyst.

SECTION IX

GENITAL TUMOURS

VULVAL NEOPLASMS

I. BENIGN

1. Epithelial tumours. Papilloma, adenoma (from Bartholin gland and Skene tubule) and hidradenoma which is adenoma of sweat glands.
2. Connective tissue tumours. Lipoma, fibroma, leiomyoma, neuroma, haemangioma and lymphangioma.
3. Melanoma.

II. MALIGNANT

1. Primary tumours. Carcinoma, basal cell carcinoma (rodent ulcer), sarcoma and melanoma.
2. Secondary tumours. The primary may be in the ovary, body of uterus or vagina. The lesion is due to retrograde vascular or lymphatic spread. Secondaries of choriocarcinoma are dark red in colour.

VULVAL INTRAEPITHELIAL NEOPLASIA (VIN)

PATHOLOGY

VIN is classified according to the histological findings in the biopsy specimen into 3 grades:

- VIN I (mild dysplasia or atypia). The lower third of the epithelium is replaced by undifferentiated cells.
- VIN II (moderate dysplasia or atypia). The lower two-thirds of the epithelium are replaced by undifferentiated cells.
- VIN III. It includes severe dysplasia or atypia and carcinoma in situ. In severe dysplasia more than two-thirds of the epithelium are replaced by undifferentiated cells, but still there are some mature cells on the surface. In carcinoma in situ the whole thickness of the epithelium is replaced by undifferentiated cells but there is no invasion below the basement membrane. Because it is difficult to differentiate between severe dysplasia and carcinoma in situ and because both lesions have the same prognosis, both conditions are referred to as VIN III.

Note. The undifferentiated cells show abnormal nuclei (atypia). The nuclei are large, irregular in size and shape, hyperchromatic with dense chromatin clumping, with large nucleoli and abnormal mitotic figures. The nucleo-cytoplasmic ratio is increased. There is loss of stratification of cells.

CLINICAL PICTURE

The average age of VIN is 40 years (20-30 years less than the age of invasive carcinoma). The patient may complain of pruritus or soreness of the vulva. However, about 50% of the patients are asymptomatic. The vulva may look normal or show bright red, dark red, brown, grey, or white areas (due to hyperkeratosis). In most cases (more than two-thirds) the disease is multifocal. It may affect several areas on the vulva and may also affect the perianal area, the vagina and the cervix. So the whole lower genital tract must be properly examined.

DIAGNOSIS

Biopsy taken from abnormal areas is essential for diagnosis. The colposcope or toluidine blue test can help to identify the abnormal areas for biopsy. Toluidine blue solution 1% is applied and left for 3 minutes then washed with 1% acetic acid. Abnormal areas remain blue in colour (Collins test). Toluidine blue is a nuclear stain.

TREATMENT

1. Local excision of the affected area with a generous margin of healthy skin (at least 0.5-1 cm).
2. Simple vulvectomy may be done for extensive lesion, if the patient is over 50 years.
3. Skinning vulvectomy. The vulval skin is removed without the subcutaneous tissues followed by skin graft (from thigh or buttock). Indicated for extensive lesion in a young patient to avoid the complications of simple vulvectomy which include disfiguring, dyspareunia, decreased sexual arousal, loss of libido and psychological disturbances.
4. Laser vaporization or excision.

The disease is liable to recur in 30-50% of cases and long term follow-up is necessary.

PAGET DISEASE OF THE VULVA

Pathology

It is a specific type of intraepithelial neoplasia. It is characterized by the presence of Paget cells in the epidermis. These are large round or oval secretory cells with large central and hyperchromatic nuclei. The cytoplasm is pale and vacuolated due to the presence of mucin. The cells are initially found in the basal layer of the epidermis but finally involve the whole thickness of the epithelium, i.e. adenocarcinoma in situ. In about 20% of cases the underlying sweat glands show an adenocarcinoma. In Paget disease of the nipple of the breast there is an underlying ductal carcinoma in almost 100% of cases.

Clinical Picture

Most cases occur in menopausal and postmenopausal women. The patient may complain of local pain, pruritus or the presence of a vulval lesion. The lesion is hyperaemic, sharply demarcated and thickened with foci of induration and excoriation. The hyperaemic area may

be covered with white areas giving the picture of "cake icing" which is pathognomonic of Paget disease.

Treatment

It is by a wide local excision. The specimen must be examined histologically with great care to exclude an underlying apocrine adenocarcinoma.

Note. VIN includes both the squamous VIN (VIN I, II and III) and non-squamous VIN which is Paget disease (adenocarcinoma in situ).

INVASIVE VULVAL CARCINOMA

PATHOLOGY

Incidence. Vulval carcinoma is rare and accounts for about 4% of all malignant lesions in the female genital tract. The incidence is around 3 per 100,000 per year.

Age. The commonest age incidence is 60-70 years. It is primarily a disease of postmenopausal women.

PREDISPOSING FACTORS

1. Any longstanding irritative agent, chemical, mechanical or infective. Syphilis, granuloma venereum, lymphogranuloma venereum, and human papillomavirus infection predispose to the lesion.
2. Pruritus vulvae.
3. Vulval dystrophy which is found in 50% of cases.
4. Immune deficiency. Patients with acquired immune deficiency syndrome (AIDS) and those with organ transplant are liable to have different types of cancer.
5. Diabetes mellitus is present in about 10% of cases, obesity and hypertension in 30-50% of cases. So some type of endocrinopathy may predispose to the disease.
6. Smoking.

SITES

Any part of the vulva can be affected. The commonest sites in decreasing order of frequency are, labia majora, clitoris and labia minora.

MACROSCOPIC APPEARANCE

(1) Cauliflower mass; (2) malignant ulcer with everted edges and indurated base; (3) nodular masses; (4) raised plaques. Multiple growths may occur and sometimes there are labial kissing ulcers which are due to lymphatic spread, or direct contact, or due to multifocal disease.

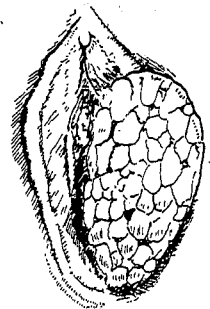


Fig.79. Vulval carcinoma

MICROSCOPIC APPEARANCE

(1) Squamous cell carcinoma in the majority of cases (90%); (2) adenocarcinoma may arise in Bartholin gland or paraurethral ducts (1-2%); (3) malignant melanoma (8-10%). It is the second most common type; (4) verrucous carcinoma.

MODE OF SPREAD

1. Direct spread to urethra, bladder, vagina, perineum, anus or groin.
2. Lymphatic spread to inguinal and femoral lymph nodes on both sides because there is crossing of lymphatics. These groin glands drain into the lymph node of Cloquet (Rosenmuller) found in the femoral canal → external iliac glands → common iliac glands → aortic glands.
3. Haematogenous spread to liver, lungs, brain and bone is uncommon.
4. Implantation or direct contact leading to kissing ulcers (doubted).

FIGO STAGING

The International Federation of Gynaecology and Obstetrics (FIGO) in 1994 classified squamous cell carcinoma of the vulva into the following stages:

- Stage 0: Intraepithelial carcinoma (carcinoma in situ).
- Stage I: Tumour confined to the vulva and/or perineum, 2 cm or less maximum diameter. No nodal metastasis.
- IA: Stromal invasion 1 mm or less.
- IB: Stromal invasion more than 1 mm.
- Stage II: Tumour confined to the vulva and/or perineum, more than 2 cm maximum diameter. No nodal metastasis.
- Stage III: Tumour of any size with spread to any of the following: Lower urethra, vagina, anus or unilateral regional lymph node metastasis.
- Stage IV A: Tumour of any size with spread to any of the following: Upper urethra, bladder mucosa, rectal mucosa, pelvic bone or bilateral regional lymph node metastasis.
- Stage IV B: Any distant metastasis including pelvic lymph nodes.

CAUSES OF DEATH

(1) Malignant cachexia; (2) infection; (3) haemorrhage; (4) thrombophlebitis and pulmonary embolism; (5) complication of treatment, the mortality rate of radical vulvectomy is 1-3%.

DIAGNOSIS

The patient may complain of one or more of the following: (1) a mass or ulcer; (2) pain and pruritus vulvae; (3) purulent or bloody discharge. About 20% of patients will have no complaint and the tumour is found incidentally during routine pelvic examination. Biopsy under anaesthesia confirms the diagnosis and must be done in every case. Pap smear should be taken from the cervix, and colposcopy of the cervix and vagina should be performed

because of the common association of vulval cancer with other intraepithelial or invasive carcinoma of the cervix or vagina.

TREATMENT

I. Surgery

Surgery is the primary treatment. The operation is radical vulvectomy with removal of the inguinal and femoral lymph nodes on both sides including the lymph node of Cloquet. The pelvic lymph nodes receive postoperative irradiation in the following situations.

1. The gland of Cloquet shows invasion.
2. Two or more of the groin glands are infiltrated or if one node is totally replaced by the tumour, or there is spread outside its capsule.
3. The tumour is large and more than 4 cm in diameter.
4. Involvement of the clitoris, urethra, vagina, and anus as these midline structures drain directly into the pelvic nodes.

Pelvic exenteration combined with radical vulvectomy and bilateral groin lymphadenectomy is performed if the bladder or rectum is involved. Excision of pelvic bone is done if the bone is infiltrated.

Conservative Surgery

1. Stage I with the lesion situated laterally. Hemivulvectomy with removal of the ipsilateral inguinofemoral nodes might be done.
2. Stage IA with a solitary lesion showing invasion of 1 mm or less below the basement membrane of the epithelium. This microinvasive carcinoma might be treated by wide local excision with a safety margin of 3 cm all around without removal of the groin nodes. With this microinvasion there is no risk of lymph node involvement. However, the recurrence rate is high (13%).

The aim of conservative surgery is to reduce both physical and psychological morbidity which result from radical vulvectomy.

Preoperative Evaluation of the Patient

This includes:

1. Chest x-ray.
2. Intravenous pyelogram.
3. Cystoscopy, sigmoidoscopy and barium enema if we suspect invasion of bladder or rectum.
4. Liver scan in case of malignant melanoma which spreads early by the blood stream. This is done using ultrasound, CT scan, or MRI.
5. Laboratory tests: (a) Complete blood count; (b) urinalysis; (c) renal function tests; (d) liver function tests; (e) fasting blood sugar; (f) serum electrolytes;

6. Electrocardiogram.

At least 4 units of blood are cross-matched and made available for transfusion.

Operative Complications

1. Shock.
2. Haemorrhage (primary, reactionary and secondary).
3. Infection of the wound and osteitis of the pubic bone.
4. Venous thrombosis and pulmonary embolism.
5. Injury of femoral vessels.
6. Fluid and electrolyte disturbances.
7. Necrosis of the skin edges.
8. Breakdown of the wound. Wound separation is the commonest complication and occurs in about 30-50% of cases.
9. Chronic lymphoedema of the legs (about 30%).
10. Groin seroma (lymphocyst formation).
11. Vaginal stenosis.
12. Genital prolapse, particularly the posterior vaginal wall due to loss of perineal support.
13. Urinary incontinence, misdirection of urinary stream, and chronic urinary infection due to urethral damage.
14. Inguinal and femoral hernia.
15. Damage of femoral nerve and paraesthesia over the front of the thigh (L-1 and L-2).
16. Distortion of the vulva is inevitable and may cause dyspareunia, decreased sexual arousal, and loss of libido.
17. Primary mortality occurs in 1-3% of cases due to shock, haemorrhage, infection, and pulmonary embolism.

II. Radiotherapy

The tumour is radioresistant and the tissues of the vulva cannot tolerate radiation and the surrounding skin will undergo excessive necrosis. So radiotherapy is indicated if the patient is not fit for surgery, or the tumour is inoperable, and when the patient refuses surgery, and for recurrent tumour. Postoperative radiation of the pelvis is indicated in certain cases to avoid the risk of pelvic lymphadenectomy.

III. Chemotherapy

Metastatic or recurrent melanoma is treated by cytotoxic drugs as hydroxyurea and vincristine. Also cytotoxic drugs can be combined with radiotherapy to treat locally advanced squamous cell carcinoma.

IV. Laser and Diathermy Coagulation

A palliative measure for inoperable and recurrent cases to keep the growth in check.

PROGNOSIS

The 5-year survival rate is approximately 90% for Stage I, 80% for Stage II, 50% for Stage III, and 20% for Stage IV.

Cancer of the clitoris carries a bad prognosis because of rich blood vessels and lymphatics allowing early spread of the tumour, also the spread is direct to the deep femoral node of Cloquet, however, recent studies did not confirm this.

OTHER MALIGNANT VULVAL TUMOURS

MALIGNANT MELANOMA

It is the second most common malignant vulval tumour and accounts for 8-10% of cases. It may arise de novo or from pre-existing nevi.

Treated by radical vulvectomy and bilateral inguinofemoral lymphadenectomy. As the prognosis is poor due to early spread by bloodstream, some treat this lesion by vulvectomy alone. The prognosis is related mainly to the depth of invasion into the dermis. Metastatic or recurrent malignant melanoma is treated by chemotherapy. The 5-year survival rate is about 50%.

ADENOCARCINOMA OF BARTHOLIN GLAND

It is a rare tumour (1-2%) which is treated by radical vulvectomy and bilateral inguinofemoral lymphadenectomy. An enlargement of Bartholin gland in a postmenopausal patient should be considered malignant and the gland must be removed.

VERRUCOUS CARCINOMA

It is a papillary squamous cell carcinoma. It is rare. Macroscopically and microscopically it resembles condyloma acuminatum and diagnosis can be difficult. The tumour may occur in the cervix, vagina, and vulva. It is locally malignant and metastases to groin lymph nodes do not occur, so the treatment is wide local excision or vulvectomy without lymphadenectomy. Radiotherapy is contraindicated as it is ineffective and may induce anaplastic changes and rapid invasion.

BASAL CELL CARCINOMA

A rare tumour which is locally malignant and does not metastasize. It appears as a white nodule or plaque. Treatment is by local excision.

VULVAL SARCOMA

It is responsible for less than 1% of vulval malignancies. It occurs in young patients and the mean age is 40 years. Histologic types include leiomyosarcoma (commonest type), fibrosarcoma, liposarcoma, angiosarcoma, neurofibrosarcoma, and rhabdomyosarcoma. It is treated like invasive carcinoma, by radical vulvectomy and bilateral inguinofemoral lymphadenectomy.

VAGINAL NEOPLASMS

BENIGN NEOPLASMS

Types

1. Papilloma. In most cases the papilloma is a skin tag resulting from obstetrical or surgical trauma. However, a true papilloma can occur. Other types of papilloma are due to infection with human papillomavirus (condylomata acuminata) or due to bilharziasis.
2. Angioma.
3. Adenoma. It arises from Gartner duct, or remains of Müllerian ducts.
4. Fibroma and Lipoma. Arise from the paravaginal tissues (paracolpos) and can reach a large size.
5. Myxoma. The tumour consists of myxomatous and fibrous or fatty tissue (fibromyxoma or lipomyxoma). Arises from the paracolpos.
6. Granuloma. It consists of granulation tissue found in vaginal scars as those following total hysterectomy and colporrhaphy.
7. Adenosis. Vaginal adenosis means the presence of columnar (glandular) epithelium in the vaginal mucosa. This columnar epithelium may resemble tubal epithelium (tubal adenosis) or endometrium (endometrial adenosis) or endocervical epithelium (endocervical adenosis). Vaginal adenosis occurs in women whose mothers received diethylstilboestrol during pregnancy and also in women who were not exposed to the drug. The areas of adenosis appear as red, friable and velvety tissue on the cervix or vagina. The lesions bleed easily and do not stain with iodine (due to absence of glycogen). Adenosis may give rise to clear cell adenocarcinoma.

MALIGNANT NEOPLASMS

A. Primary Tumours

Carcinoma, sarcoma, and melanoma.

B. Secondary Tumours

These are more common than primary tumours. So with vaginal malignancy we should exclude a primary tumour elsewhere. The mechanisms of spread are (1) direct extension from cervix, vulva, urethra, bladder or rectum; (2) retrograde lymphatic spread from endometrial carcinoma; (3) haematogenous spread from a primary tumour in the breast, kidney, ovary or any other organ. Retrograde vascular spread may occur with choriocarcinoma; (4) seeding. Cells from endometrial carcinoma may become implanted in the vaginal vault after hysterectomy.

CARCINOMA OF THE VAGINA

A. VAGINAL INTRAEPITHELIAL NEOPLASIA (VAIN)

Like vulval and cervical intraepithelial neoplasia, the lesion is classified according to the histological findings in the biopsy specimen into Grade I (mild dysplasia), Grade II (moderate dysplasia) and Grade III (severe dysplasia and carcinoma in situ). VAIN has a localized or patchy distribution (unifocal or multifocal). The commonest site is the upper third of the vagina. It may be associated with similar lesions on the cervix or vulva.

Symptoms

In most cases, VAIN is asymptomatic, however, some patients complain of vaginal discharge, vaginal spotting or dyspareunia.

Signs

The vaginal mucosa may show red areas but in most cases the mucosa looks normal and the condition is discovered accidentally as a result of routine vaginal cytology. Diagnosis is confirmed by colposcopic examination of the vagina and biopsy is taken from abnormal areas. If the colposcope is not available we do Schiller iodine test to identify abnormal areas which remain unstained.

Treatment

I. Unifocal lesion.

1. Local excision with a safety margin of healthy tissue all around (at least 0.5-1 cm). A scalpel or electrosurgical loop is used.
2. Laser vaporization, using carbon dioxide laser.
3. Destruction by electrocautery. Cryocautery is not used as it may lead to necrosis of adjacent tissues as the vaginal wall is thin.

II. Multifocal lesions:

1. Laser vaporization.
2. Vaginectomy total or partial.

B. INVASIVE VAGINAL CARCINOMA

Pathology

Incidence. About 1-2% of malignant neoplasms of the female genital tract. The incidence is less than 1 per 100,000 women per year.

Age. The commonest age incidence is 60-80 years.

Predisposing Factors

Human papillomavirus infection, chronic vaginal irritation, e.g. neglected vaginal pessary, and low socioeconomic state.

Macroscopic Appearance

1. Cauliflower carcinoma.
2. Malignant ulcer.
3. Diffuse infiltrative type.

Microscopic Appearance

1. Squamous cell carcinoma in the majority of cases (more than 90%)
2. Adenocarcinoma is rare because the vagina is devoid of glands. It arises from Gartner duct or remains of müllerian ducts.
3. Clear cell adenocarcinoma seen in young women whose mothers received diethylstilboestrol during pregnancy.
4. Verrucous carcinoma which is a papillary squamous cell carcinoma.
5. Small cell carcinoma.
6. Melanocarcinoma.

Mode of Spread

1. Direct spread; forward to the bladder and urethra, backward to the rectum, upward to the cervix, downward to the vulva, and laterally into the parametrium. For the purpose of international classification any growth showing involvement of another organ as bladder, urethra, cervix, or vulva should be classified as originating from this organ. So a growth involving vagina and cervix is considered a cervical tumour.
2. Lymphatic spread. Carcinoma of the upper two-thirds of the vagina, which are derived from müllerian ducts, spreads like carcinoma of cervix, that of the lower third, which is derived from the urogenital sinus, spreads like carcinoma of the vulva.
3. Haematogenous spread. Distant metastases to liver and other organs are rare.

FIGO Staging

- Stage 0:** Intraepithelial carcinoma (carcinoma in situ).
- Stage I:** Invasive carcinoma limited to vaginal wall.
- Stage II:** Extension to paravaginal tissues (paracolpos), but not to pelvic wall.
- Stage III:** Extension to pelvic wall.
- Stage IV:** Extension to bladder or rectal mucosa or outside the true pelvis.
- IVa:** Extension to bladder or rectal mucosa.
- IVb:** Spread outside the true pelvis (distant metastasis).

Because of the thinness of the vaginal wall, most invasive cancers are at least stage II when they are discovered.

Diagnosis

A. Symptoms

The patient may complain of one or more of the following:

1. Irregular vaginal bleeding and contact bleeding.
2. Offensive vaginal discharge due to secondary infection.
3. Vaginal mass.
4. Dyspareunia.
5. Symptoms due to spread to other organs as dysuria, dyschezia, incontinence of urine or faeces.
6. Cachexia. It occurs in advanced cases. It is due to repeated blood loss, infection, toxic absorption, pain and lack of sleep.

B. Signs

Most lesions occur in the upper third of the posterior vaginal wall. The next most frequent site is the lower anterior vaginal wall. The lesion is indurated, necrotic, and usually bleeds on touch. Rectal examination is done in posterior wall lesion to exclude extension to the rectum.

C. Investigations

1. Biopsy which is essential for diagnosis.
2. Cystoscopy for anterior wall lesion to exclude extension to bladder or urethra.
3. Sigmoidoscopy for posterior wall lesion.
4. Chest X-ray to exclude metastasis.
5. Intravenous pyelogram.
6. Computerized tomography (CT) scan to the pelvis and abdomen to detect metastases to pelvic and aortic lymph nodes and liver.
7. Magnetic resonance imaging (MRI) is more accurate than CT scan, but it is costly.
8. Laboratory tests. (a) Complete blood count; (b) urinalysis; (c) renal function tests; (d) liver function tests; (e) fasting blood sugar, and (f) serum electrolytes.
9. Electrocardiogram.

Treatment

1. Radiotherapy. It is the treatment of choice. Radium or caesium is inserted into the vagina followed or preceded by external pelvic radiation. The inguinal nodes are also irradiated if the lower third of the vagina is involved.
2. Surgery. (a) Tumours in the upper two-thirds of the vagina are treated by radical hysterectomy, pelvic lymphadenectomy, and removal of the upper part of the vagina, extending at least one inch below the growth; (b) tumours in the lower third of the vagina are treated by removal of the lower part of the vagina, plus radical vulvectomy with bilateral groin lymphadenectomy; (c) advanced cases involving the bladder or rectum are treated by pelvic exenteration (anterior, posterior, or total).

Prognosis

It is bad as the vaginal wall is thin and so the tumour invades rapidly the adjacent organs. Also the vagina is rich in blood vessels and lymphatics, so metastases occur early. The 5-year survival rate for stage I is about 70%, stage II: 50%, stage III: 30% and stage IV: 0-20%. The 5-year survival rate for all stages is 30-40%.

SARCOMA OF THE VAGINA

A very rare disease of the vagina which may occur at any age. There are two types:

1. ADULT VAGINAL SARCOMA

The tumour arises from the subepithelial connective tissue layer of the vaginal wall. It is either a spindle cell, round cell or mixed cell sarcoma.

2. GRAPE-LIKE SARCOMA OF CHILDREN

It is rhabdomyosarcoma, often referred to as sarcoma botryoides. In Greek botrys means a bunch of grapes. It arises from the subepithelial connective tissue layer of the cervix or vagina. It usually occurs in infants and young children under 3 years. The tumour forms a mass of soft pinkish polypi which resembles a bunch of grapes. It grows rapidly and may appear at the vulva. If untreated most patients die within 1 to 2 years. Histologically the tumour shows embryonal rhabdomyoblasts (primitive skeletal muscle cells) and undifferentiated round, spindle, and stellate cells. The ground substance is myxoid and jelly-like. It is treated by combination chemotherapy; a combination of vincristine, actinomycin D, and cyclophosphamide (VAC). If the tumour persists radiotherapy is given. If the tumour does not disappear surgery is done in the form of total vaginectomy and radical hysterectomy with pelvic lymphadenectomy. In fact some tumours are controlled by chemotherapy alone. The 5-year survival rate is about 80%.

Note for the postgraduate

Diethylstilboestrol (DES) is a synthetic oestrogen. It was given in the past to pregnant women having abortion, diabetes or preeclampsia to reduce fetal loss. About 2 to 3 million pregnant women received the drug between 1950 and 1970. In 1971 it was proved that the drug leads to the development of clear cell adenocarcinoma in the vagina of the female offspring at the age of 7 to 31 years, with a peak at 19 years. The drug is no more used in pregnancy.

Effects on the Female Offspring from In-utero Exposure to DES

1. Tube. Hypoplasia, and liability to ectopic pregnancy.
2. Uterus. Hypoplasia, abnormal cavity, and synechiae.
3. Cervix. Hypoplasia, incompetent cervix, cervical erosion, concentric cervical rings, and clear cell adenocarcinoma.
4. Vagina. Hypoplasia, obliteration of vaginal fornices, transverse vaginal ridges, vaginal adenosis, and clear cell adenocarcinoma.
5. Physiologic abnormalities. Hypomenorrhoea, primary dysmenorrhoea, infertility, ectopic pregnancy, abortion, and preterm labour (patulous cervix).

CERVICAL NEOPLASMS

I. Benign.

Papilloma, adenoma, fibroadenoma, leiomyoma, angioma, and condylomata acuminata.

II. Malignant:

A. Primary tumours:

1. Carcinoma.
2. Sarcoma. Fibrosarcoma, leiomyosarcoma and grape-like sarcoma of children (sarcoma botryoides).
3. Carcinosarcoma.
4. Melanoma.
5. Lymphoma.

B. Secondary tumours.

CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)

PATHOLOGY

Incidence. About 200 per 100,000 females per year.

Age. The average age is 35 years.

Aetiology. The cause of cervical cancer is unknown, but certain predisposing factors are recognized which are discussed with invasive cervical carcinoma.

MACROSCOPIC APPEARANCE

CIN cannot be seen by the naked eye. The cervix looks normal or may show an associated nonspecific lesion as erosion (ectopy), cervicitis, or leucoplakia.

MICROSCOPIC APPEARANCE

CIN (like vulval and vaginal intraepithelial neoplasia) is classified into 3 grades:

1. CIN I (mild dysplasia). The lower third of the epithelium is replaced by undifferentiated cells.
2. CIN II (moderate dysplasia). The lower two-thirds of the epithelium are replaced by undifferentiated cells.
3. CIN III. It includes severe dysplasia and carcinoma in situ. In severe dysplasia more than two-thirds of the epithelium are replaced by undifferentiated cells, but still there are some mature cells on the surface. In carcinoma in situ the whole thickness of the epithelium is replaced by undifferentiated cells but there is no invasion below the basement membrane. Because it is difficult to differentiate between severe dysplasia and carcinoma in situ and because both lesions have the same prognosis, both conditions are referred to as CIN III.

THE BETHESDA SYSTEM

This system (squamous intraepithelial lesion) is used in the USA and is classified into:

1. Low grade squamous intraepithelial lesions (LSIL) which correspond to CIN I and human papillomavirus changes.
2. High grade squamous intraepithelial lesions (HSIL) which correspond to CIN II and III lesions.

COURSE OF CIN

CIN may regress, persist and remain unchanged, or progress to invasive carcinoma. The latter takes about 10 years (1-15 years). The percentage of cases becoming invasive is about 15% for CIN I, 25% for CIN II, and 50% for CIN III.

DIAGNOSIS

CIN has no symptoms. There are no characteristic signs as the lesion is not seen by the naked eye. The cervix looks normal, or may show an associated nonspecific lesion as erosion, cervicitis, or leucoplakia. The diagnosis is made by the routine cervical smear. If the smear shows abnormal cells the diagnosis must be confirmed by cervical biopsy. This is done using the colposcope to select the site for biopsy. If the colposcope is not available we do Schiller iodine test to select the site for biopsy. If the smear is positive and no lesion could be seen by these methods a cone biopsy is done.

Cervical Smear

A wooden spatula (Ayre) or plastic one (Rolon) is rotated 360° to scrape the lower part of the cervical canal and the portio vaginalis at the external os (squamocolumnar junction where carcinoma mostly arises). The cytobrush can be used to collect the specimen (this is the most effective method of cervical sampling). The specimen is spread on a slide and immediately fixed (in less than 10 seconds) by immersion into absolute alcohol (95%) or by spraying with a mixture of alcohol and carbowax (to prevent air-drying). The smear is stained with Papanicolaou stain. The cervical smear is done for all sexually active women and repeated every year in high risk patients and every three years in low risk patients. This is the practice in the USA, but in the UK the figures are 3 and 5 years. High risk factors include starting coitus before the age of 20 years, multiple sexual partners, infection with human papillomavirus, and smoking.

Notes

- Some centers obtain 3 specimens; from posterior fornix of the vagina (V), cervix (C) and endocervix (E).
- The abnormal appearance of cells in the cervical smear is described as dyskaryosis, mild, moderate, and severe (cytological diagnosis). The abnormal appearance of cells in the biopsy specimen is described as dysplasia (histological diagnosis).

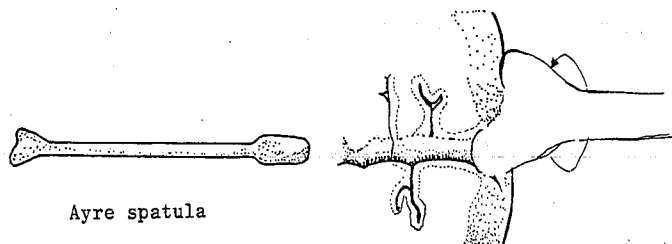


Fig.80 Cervical smear

The Colposcope

It magnifies the cervix 10 to 40 times to allow study of lesions not seen by the naked eye and to select the site for biopsy. Endocervical curettage must be done during colposcopic examination. Curettage is done without anaesthesia, using a small curette.

Schiller Iodine Test

The cervix is painted with iodine solution (Schiller, Gram or Lugol iodine solution). The solution is swabbed after half a minute. Normal healthy squamous epithelium contains glycogen and so stains dark brown. Abnormal areas, e.g. ulcer, erosion (columnar epithelium) and cancer remain unstained due to absence of glycogen.

The test is indicated if the cervical smear is positive but the colposcope is not available to select the site for biopsy. All unstained areas should be biopsied. Endocervical curettage is also done.

Cervical Biopsy

This must be done to confirm the diagnosis of CIN and to exclude invasion. It is carried out using the colposcope. Cervical biopsy is of two types.

- a. Punch biopsy. It is taken from all suspected areas and is preferable to include an area of healthy tissue for comparison.
- b. Cone biopsy. The indications of conization are:
 1. The lesion extends into the cervical canal and its limit cannot be seen by the colposcope.
 2. The whole squamocolumnar junction cannot be visualized.
 3. The cervical smear is positive and no lesion can be seen by the colposcope.
 4. When invasive carcinoma is diagnosed or suspected by cytology, punch biopsy or colposcopy.
 5. If endocervical curettage is positive for abnormal cells.
 6. The colposcope is not available and no lesion is seen by Schiller iodine test.

The limits of the base of the cone are determined by the colposcope or Schiller iodine test so that the incision must include all abnormal areas on the portio vaginalis, and the apex of the cone reaches just below the internal cervical os to include the whole endocervical

epithelium. The cone is divided into many serial sections (average 75 slices) for microscopical examination. Complications include primary and secondary haemorrhage, infection, cervical stenosis which may lead to infertility, dysmenorrhoea, haematometra, and cervical dystocia during labour. It may also lead to incompetent cervix with recurrent abortions or preterm labour.

Cervicography

A special camera is used to photograph the cervix after application of acetic acid. The film is sent to be examined by an expert. Resorted to if a colposcope is not available.

TREATMENT

- I. Destruction of the lesion and whole transformation zone. This is achieved by cryocautery, electrocautery, diathermy cautery, cold coagulation or laser. The cure rate is about 95%. Cold coagulation is a misnomer as the technique destroys tissues by heat, but it is cold relative to the high temperature of electrocautery. The temperature reaches only 100° C.
- II. Excision of the lesion and whole transformation zone. This is carried out by laser, or by a diathermy needle, or by a diathermy loop. It is done under general or local anaesthesia using the colposcope.
- III. Conization. The cure rate is 99%. It is superior to local destruction and is carried out where the lesion extends into the cervical canal, and its extent is not visible by the colposcope.
- IV. Hysterectomy. It is rarely done. The indications are: (1) women above 40 years; (2) patients requesting sterilization; (3) the presence of associated pathology needing hysterectomy as fibroids; (4) when it is difficult to follow up the patient by cytology or colposcopy; (5) residual lesion after treatment. However, residual disease can be treated by repeating local destruction, local excision, conization or hysterectomy; (6) if the lesion involves the upper vagina. Treatment is hysterectomy with removal of upper part of vagina. Alternative to this is conization and laser destruction of the vaginal lesion.

Some gynaecologists treat CIN I conservatively. In this case cervical smear is repeated every 6 months, and any associated infection is treated. CIN I becomes invasive in about 15%, regresses in about 30%, and remains unchanged in the rest.

FOLLOW-UP

Follow-up by cytology every 3 months for one year and then every 6 months for 5 years and then yearly indefinitely.

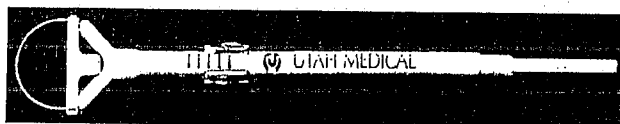


Fig. 80-1. Diathermy excision loop

INVASIVE CERVICAL CARCINOMA

PATHOLOGY

Incidence. It varies between 15 to 35 per 100,000 females per year. It varies considerably from country to country and from race to race.

Age. The commonest age incidence is 45-55 years. The tumour, however, can occur at any age and it is reported that there is another peak at the age of 35.

Aetiology. The cause of cervical cancer is unknown, but the following are predisposing factors.

1. **Coitus.** Coitus starting at an early age, i.e. before the age of 20 years is the most important predisposing factor. Also the presence of many sexual partners, so the lesion is more common in prostitutes and rare in virgins. Male promiscuity is also a factor. The cervical epithelial cells normally phagocytose spermatozoa. This provides the cells with large quantities of nucleic acids and stimulates abnormal epithelial activity. It is also suggested that an agent is transmitted from the male during coitus which may be responsible.
2. **Infection** with the human papillomavirus (particularly subtypes 16 and 18, and less frequently subtypes 31, 33 and 35).
3. **Immune deficiency.** Patients with acquired immune deficiency syndrome (AIDS), and those with organ transplant are more liable to have different types of cancer.
4. **Parity.** More common in multiparae (95%). High parity indicates frequent coitus during many years.
5. **Social and economic state.** The disease is more common among lower classes due to early marriage, high parity and frequent coitus.
6. **Race.** The incidence is low among Moslem and Jewish women. This is related to genetic and racial factors and not to the practice of male circumcision. It was believed that circumcision prevents irritation of the cervix by the smegma which is carcinogenic. However, this is not true.
7. **Vitamin deficiency.** Lack of vitamin A, C, E and folic acid has been suggested.
8. **Combined oral contraceptives taken for a long period (more than 10 years).** A matter of controversy. However, patients on the pills are followed by cervical smear. If there is a relation, pills lead to cervical adenocarcinoma.
9. **Exposure in utero to diethylstilboestrol.** This drug is no more used.
10. **Smoking.** Products of smoking are concentrated in cervical mucus and may produce changes in the DNA of cervical cells. Also smoking lowers the serum levels of some vitamins. Smoking predisposes to squamous cell carcinoma.

SITES

1. Carcinoma of the portio vaginalis or ectocervical carcinoma (90%). It arises from the squamous epithelium covering the vaginal portion of the cervix and always starts at or near the squamocolumnar junction at the external os (transformation zone).

2. Endocervical carcinoma (10%). It arises from the columnar epithelium lining the cervical canal or cervical glands.

Carcinoma of the Portio Vaginalis

Macroscopic Appearance

1. Cauliflower carcinoma (exophytic or hypertrophic type). There is a fungating mass projecting into the vagina. The base is indurated, the surface friable, the mass is infected and necrotic and bleeds on touch. It is the commonest type.
2. Ulcerative carcinoma (endophytic type). It forms a malignant ulcer with a raised everted edge and indurated base.
3. Nodular carcinoma. Appears as a firm nodule on the cervix but finally ulceration occurs.
4. Infiltrative carcinoma. There is a gradual fibrosis of cervical tissue due to malignant infiltration. The lesion shows a puckered surface with a very hard base. Fibrosis leads to contraction of the vaginal vault.

Microscopic Appearance

Carcinoma of the portio vaginalis is a squamous cell carcinoma in the majority of cases (90%), occasionally it is an adenocarcinoma which arises from the columnar epithelium covering an erosion.

Endocervical Carcinoma

Macroscopic Appearance

In early cases the cervix looks normal but as the tumour grows the cervix becomes distended and barrel-shaped. After sometime the tumour grows out from the external os.

Microscopic Appearance

Endocervical carcinoma is an adenocarcinoma in 50% of cases, and squamous cell carcinoma in 50% due to metaplasia of the columnar epithelium into squamous epithelium as a result of chronic cervical infection.



Fig.81. Cauliflower carcinoma

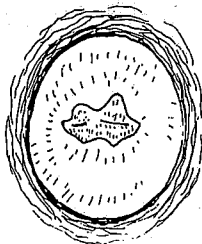


Fig.82. Ulcerative carcinoma

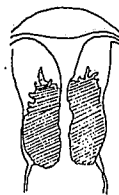


Fig.83. Endocervical carcinoma

Notes

- 80% of all cases of cervical carcinoma are squamous cell carcinoma and 20% are adenocarcinoma.
- Rare types of carcinoma include verrucous carcinoma, clear cell adenocarcinoma, papillary serous adenocarcinoma, endometrioid adenocarcinoma, adenosquamous carcinoma, small cell carcinoma and metastatic carcinoma.

HISTOPATHOLOGY

Squamous cell carcinoma of the cervix is classified into 3 grades:

Grade 1. The tumour is well differentiated. It is the least malignant.

Grade 2. The tumour is moderately differentiated.

Grade 3. The tumour is poorly differentiated. The most malignant.

Another classification is that of the World Health Organization (WHO) which subdivides the tumours into 3 groups:

1. The large cell nonkeratinizing tumour. This has the best prognosis. The normal cervical squamous epithelium is nonkeratinized.
2. The large cell keratinizing tumour with intermediate prognosis.
3. The small cell tumour which carries the worst prognosis.

Regarding prognosis, the clinical stage of the disease (extent) is more important than the type of cell or degree of differentiation. Also the tumour size affects the prognosis.

MODE OF SPREAD

1. **Direct spread.** Downwards into the vagina, upwards into the body of uterus, forwards into the bladder, backwards along the uterosacral ligaments to involve the rectum, laterally into the parametrium where it may cause ureteric obstruction by compression leading to hydronephrosis and finally renal failure and uraemia which is the commonest cause of death.
2. **Lymphatic spread.** It occurs early in the disease by both embolism and permeation. The lymph nodes affected are: (a) the paracervical gland at the crossing of the ureter and the uterine artery; (b) the external iliac glands; (c) the internal iliac (hypogastric) glands; (d) the obturator glands, 1-3 in number, near the obturator foramen; (e) the sacral lymph nodes, in the sacral concavity and on the promontory. The lymph vessels run in the uterosacral ligaments to reach these glands; (f) the hypogastric and external iliac glands drain into the common iliac glands which drain into the lower aortic lymph glands; (g) rarely the inguinal lymph nodes due to retrograde

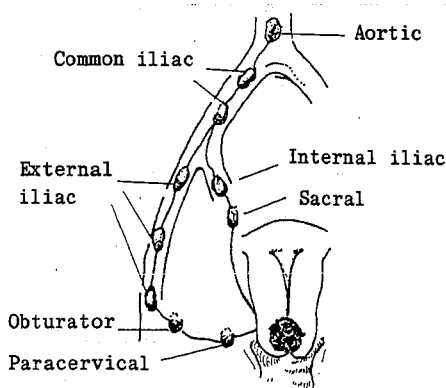


Fig. 84. Lymphatic spread of cervical carcinoma

lymphatic spread from external iliac glands. The paracervical lymph gland drains into the obturator glands which drain into the external iliac glands. The sacral nodes drain into the aortic nodes.

3. **Bloodstream:** Spread by bloodstream to distant organs as liver, lungs, brain and bones occurs late when the disease is advanced.
4. **Surface implantation (seeding):** Malignant cells may be implanted in the vagina, vulva, pelvic cavity or abdominal wall during Wertheim operation. Wertheim clamps are used during operation to close the vagina to prevent this surface implantation which is very rare.
5. **Intraperitoneal metastases.** This may occur in advanced disease when the tumour erodes through the posterior wall of the cervix.

Note. The occurrence of distant metastases in absence of lung involvement is explained by transfer of malignant cells by the vertebral plexus of veins.

CAUSES OF DEATH FROM CERVICAL CANCER

(1) Uraemia, the commonest cause of death (50%), due to bilateral ureteric obstruction and urinary tract infection; (2) malignant cachexia; (3) infection as parametritis, peritonitis or septicaemia; (4) severe haemorrhage from eroding a big vessel; (5) pulmonary embolism due to infection and thrombophlebitis; (6) metastases in vital organs as liver or brain; (7) complication of treatment, the primary mortality from Wertheim operation is about 1% and from radiotherapy is less than 1%.

DIAGNOSIS

A. Symptoms

The early stage of invasive carcinoma of the cervix usually does not cause symptoms and is only discovered accidentally during pelvic examination or as a result of routine screening with cervical smear. However, the patient may complain of one or more of the following:

1. **Vaginal bleeding.** It is usually the first symptom. It starts as contact bleeding occurring after coitus, douching or vaginal examination. Later on the bleeding is irregular and variable in amount. Severe haemorrhage from erosion of a big vessel is rare.
2. **Vaginal discharge.** At first, it is slight and watery, later on it becomes blood stained and offensive due to ulceration and infection and may contain necrotic debris. It is the second commonest symptom.
3. **Vaginal mass and dyspareunia.**
4. **Pain.** It is a late symptom. It is due to involvement of the tissues outside the cervix by cancer or infection. It may be in the form of (a) suprapubic pain due to pyometra; (b) pain in the iliac fossa due to parametritis; (c) pain in the loin and renal colic due to ureteric obstruction; (d) spread to urinary bladder leads to painful micturition, haematuria and fistula; (e) spread to the rectum leads to painful defaecation, bleeding per rectum and fistula; (f) pain may refer along sciatic or obturator nerve due to compression (infiltration

of nerve sheaths does not occur); (g) backache due to metastases in vertebral column or infiltration of uterosacral ligaments.

5. **Cachexia.** It occurs in advanced cases. It is due to repeated blood loss, infection, toxic absorption, pain, and loss of sleep.
6. **Other symptoms.** As symptoms of uraemia, haemoptysis and jaundice due to secondaries.

B. Signs

1. **General examination.** This may show cachexia, evidence of uraemia, left supraclavicular or inguinal lymph nodes metastases, and oedema of lower limbs which indicates lymphatic obstruction in the pelvis.
2. **Abdominal examination.** The abdomen should be carefully examined for enlarged liver, kidneys, abdominal masses, and ascites.
3. **Pelvic examination:**
 - a. Digital palpation. A malignant lesion is characterized by induration at the base, friability on the surface, bleeding on touch, necrosis and infection.
 - b. Bimanual examination. This may show cervical enlargement, limited mobility of the cervix, associated lesions in the uterus, tubes or ovaries and induration or nodularity of the parametrium. Induration may be due to malignant infiltration or infection. In such case, antibiotics are given and re-examination is performed after one week. Mobility of the cervix is tested for by moving the cervix by the fingers from side to side and by trying to pull it down by a volsellum.
 - c. Speculum examination. The lesion appears in the form of a nodule, cauliflower mass or ulcer. In case of endocervical carcinoma the cervix is distended and barrel-shaped or looks normal. In the latter case the passage of a uterine sound into the cervical canal may cause bleeding due to friability of the tissues.
 - d. Rectal examination. Must be done in every case to detect infiltration of parametrium, uterosacral ligaments and spread to the rectum. The uterosacral ligaments are better felt per rectum.

C. Investigations

1. Cervical biopsy. It must be done in every case to confirm the diagnosis and to classify the tumour according to its degree of malignancy. A punch or a wedge biopsy is taken and it is preferable to include an area of healthy tissue for comparison. Fractional curettage is done if we suspect endocervical carcinoma.
2. Examination under general anaesthesia must be done to determine the extent of the growth. It is essential for clinical staging.
3. Cystoscopy to diagnose infiltration of the bladder. Done as a routine in every case.
4. Sigmoidoscopy or barium enema if there are bowel symptoms as pain or bleeding.
5. Chest X-ray is done as a routine.

6. Intravenous pyelogram to show the condition of the ureters and kidney function. Must be done to diagnose the stage of the disease (hydronephrosis or nonfunctioning kidney indicates stage III).
7. Computerized tomography (CT) scan to the pelvis and abdomen. It shows the size of the tumour, infiltration of the parametrium, metastases in the pelvic and aortic lymph nodes and liver, and diagnoses hydronephrosis. It cannot differentiate between malignant and inflammatory nodes.
8. Magnetic resonance imaging (MRI) is more accurate than CT scan but it is costly.
9. Bone scan. Not done as a routine but only when symptoms or signs suggest metastases.
10. Estimation of serum tumour markers; cancer antigen-125 (CA-125), the squamous cell carcinoma antigen (SCCA), the carcinoembryonic antigen (CEA), and the tumour antigen-4 (TA-4) to follow response to treatment and to detect recurrence. This is rarely done due to lack of sensitivity and specificity.
11. Laboratory tests. (a) Complete blood count; (b) urinalysis; (c) renal function tests; (d) liver function tests; (e) fasting blood sugar; and (f) serum electrolytes.
12. Electrocardiogram.

General Remarks

1. Bleeding on touch is a suspicious sign of malignancy. However, it may be caused by other lesions as vascular erosion or mucous polyp.
2. Induration. The base of the lesion is firm or hard due to infiltration by malignant cells. It also occurs with infection.
3. Friability. The surface of the lesion breaks easily under the examining finger, also a blunt probe can be pushed into malignant tissue but not into healthy cervical tissue. A negative probe or Clark test does not exclude carcinoma.
4. Necrosis. The tumour grows more than its blood supply so the surface becomes ischaemic and necrotic. Ulceration and infection result after separation of the necrotic area.

Fractional Curettage

It is done to diagnose endocervical carcinoma and to differentiate it from endometrial carcinoma. The cervical canal is curetted using a small sharp curette (cervical specimen). The uterine sound is then passed followed by dilatation of the cervix and curettage of the uterine body (endometrial specimen). If the 2 specimens show malignancy the case is considered cervical carcinoma if the tumour is squamous cell carcinoma and endometrial carcinoma if it is adenocarcinoma.

CLINICAL STAGING (FIGO CLASSIFICATION, 1994)

The degree of spread of carcinoma of cervix must be determined clinically before applying any method of treatment. The aim of this clinical staging is to determine the line of treatment,

to compare the results of treatment by different methods and from different centers all over the world and to inform the patient about the prognosis.

Stage 0: Intraepithelial carcinoma (carcinoma in situ).

Stage I: Invasive carcinoma limited to the cervix or extending to the body of the uterus.

IA: Microinvasive carcinoma diagnosed only by microscopy.

IA1: Stromal invasion below the basement membrane less than 3 mm in depth and 7 mm or less in width.

IA2: Stromal invasion 3-5 mm in depth and 7 mm or less in width.

IB: Microscopic lesion greater than IA2 or clinically visible lesion limited to the cervix.

IB1: Visible lesion 4 cm or less in greatest dimension.

IB2: Visible lesion greater than 4 cm in greatest dimension.

Stage II:

IIA: Involvement of the upper two-thirds of the vagina.

IIB: Infiltration of the parametrium on one or both sides but not reaching the pelvic wall.

Stage III:

IIIA: Involvement of the lower third of the vagina.

IIIB: Infiltration of the parametrium up to the pelvic wall or cases with hydronephrosis or nonfunctioning kidney.

Stage IV:

IVA: Spread to the bladder or rectal mucosa.

IVB: Spread outside the true pelvis (distant metastasis).

Note. Bullous oedema of the bladder does not indicate spread to the bladder mucosa.

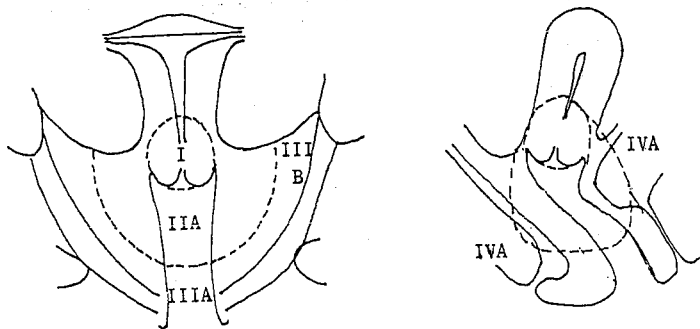


Fig.85. Clinical staging of cervical carcinoma

TREATMENT

It is prophylactic, curative, and palliative.

Prophylactic Treatment

(1) Avoidance of sexual intercourse at an early age (below 20), and multiple sexual partners; (2) the use of male or female condom; (3) a cervical smear is done for all women when they start sexual activity regardless of age, and repeated till the age of 60 years; (4) proper treatment of cervical intraepithelial neoplasia and human papillomavirus infection of the cervix; (5) if hysterectomy is needed in a patient it should be total and not subtotal (supracervical) to avoid stump carcinoma; (6) avoidance of smoking; (7) prophylactic vaccination against human papillomavirus infection is under trial.

Note. After the age of 60 years, the transformation zone becomes inactive, and lies inside the cervical canal.

Curative Treatment

This may be surgical, radiological or combined treatment. However, the treatment must be individualized.

Surgical Treatment

Stage IA1 (minimal microinvasive) is treated by simple hysterectomy or conization if the patient wants to conceive. Stage IA2 is treated by extended hysterectomy in which the medial half of each cardinal ligament is removed with the uterus and upper 2 cm of the vagina but the pelvic lymph nodes are not dissected. Stages IB and IIA are treated by Wertheim operation. It is a radical abdominal hysterectomy in which the following structures are removed: the whole uterus, both tubes and ovaries, the broad ligaments, the parametrium, all the pelvic lymph nodes, and the upper part of the vagina extending at least one inch below the growth. However, the ovaries can be spared if the patient is under 40 years. Schauta operation is a radical vaginal hysterectomy. It is less risky in obese patients but it is no more performed as it does not allow complete removal of all the pelvic lymph nodes.

Advantages of Surgery

1. Some tumours are radioresistant.
2. Operation gives better results if there is an associated pelvic lesion as fibroids, ovarian cyst or pelvic infection.
3. The ovaries can be preserved if the patient is under 40 years to avoid menopausal symptoms and risk of osteoporosis.
4. Removal of the cervix will avoid local recurrence with return of bleeding and foul discharge.
5. The remaining part of the vagina can allow for intercourse without dyspareunia.
6. Psychological advantage as the tumour is removed.

7. Early and late complications of radiotherapy are avoided.

Disadvantages

1. Wertheim operation is difficult and needs experience.
2. It is limited to certain group of patients (Stage IB and IIA).
3. The primary mortality is about 1% (higher than radiotherapy). It is due to shock, haemorrhage, infection as pelvic cellulitis and peritonitis, paralytic ileus and pulmonary embolism.
4. Injury of the bladder, ureter and rectum. Ureteric fistula occurs in about 2% of cases due to direct injury during operation or due to removal of periureteric connective tissue containing the blood supply of the ureter leading to necrotic fistula. This necrotic fistula appears 6 weeks to 6 months after operation.
5. Bladder dysfunction in the form of atony and retention of urine (commonest complication), detrusor overactivity, and stress incontinence. It is due to damage of the autonomic nerves in the pelvis.
6. Rectal dysfunction manifested by constipation.
7. Lymphocyst formation due to extensive dissection with injury of lymphatics and removal of lymph nodes. Serous fluid may collect and form a lymphocyte (lymphocele). Suction drainage of the pelvis decreases the chance of its formation
8. Venous thrombosis and pulmonary embolism which may complicate any major surgery.
9. Some patients are unfit for surgery.

Radiotherapy

It is the treatment of choice in the majority of cases. It can be used in all cases unless there is a contraindication. Radium, caesium or iridium is inserted into the uterus and lateral vaginal fornices. This is preceded or followed by external pelvic radiation.

Contraindications

1. Radioresistant tumours.
2. Radiorecurrent tumours.
3. Advanced cases with fistula or distant metastases.
4. If there is an associated pelvic lesion. Fibroids and ovarian cysts will undergo massive necrosis. Pelvic infection and pyometra will flare up with radiotherapy.
5. If the patient is young (under 35 years) because the prognosis is bad after irradiation as the tumour is usually poorly differentiated. Also in a young woman surgery is preferred to spare the ovaries to avoid menopausal symptoms.
6. Narrow vagina, stenosed cervical canal and uterine prolapse. It will be difficult to apply radium efficiently.
7. The presence of a viable fetus. The fetus is first delivered by caesarean section then irradiation is done.

Advantages of Radiotherapy (= disadvantages of surgery)

1. It is easier to apply.
2. It can be applied in advanced cases as stage III.
3. The primary mortality is low, less than 1% due to flaring up of pelvic infection leading to parametritis and peritonitis and reactionary ureteric obstruction.
4. Injury of bladder and ureter is less compared to surgery.
5. It can be used in patients who are unfit for surgery.

Disadvantages

1. Some tumours are radioresistant.
2. The cervix is not removed with liability to local recurrence with return of bleeding and foul discharge.
3. Complications may occur as injury of bladder, ureter, and rectum, depression of bone marrow with anaemia and leucopenia, vaginal stenosis and dyspareunia.
4. Ovarian function is destroyed, with appearance of menopausal symptoms in premenopausal women, and increased risk of osteoporosis.
5. Radiation-induced malignancy may occur later on in the endometrium or ovary (rare).

Combined Treatment

This gives slightly better results than surgery or radiotherapy alone.

1. Stage IB and IIA barrel-shaped endocervical carcinoma is treated by Wertheim operation. Another line of treatment is intracavitary radium and external pelvic radiation followed by simple hysterectomy as the tumour may contain central hypoxic areas which do not respond well to radiotherapy.
2. Wertheim operation is followed by radium applied in the vaginal vault or external pelvic radiation. Indicated if the specimen removed showed positive lymph nodes.
3. Chemoradiation. A combination of chemotherapy and radiotherapy is superior to radiotherapy alone. The drug commonly used is cisplatin which is given during the course of radiotherapy in advanced stages (2B, 3, and 4).

Note for the postgraduate

Radical trachelectomy and laparoscopic lymphadenectomy. Applicable to the patient with a small ectocervical carcinoma which cannot be treated safely with conization. Transvaginal radical dissection of the paracervical tissue is followed by amputation of the cervix just below the isthmus. A cerclage is done at the same time to prevent the complications of incompetent isthmus if pregnancy occurs. This is followed by laparoscopic pelvic lymphadenectomy.

Palliative Treatment

Indicated for stage IV and recurrent cases.

1. Palliative Radiotherapy

Radium is applied locally in small doses to reduce the bleeding and size of the tumour. Distant metastases and recurrent pelvic masses can receive external irradiation if radiotherapy was not previously given.

2. Palliative Surgery

a. Pelvic Exenteration (Brunchwig Operation)

- i. Anterior pelvic exenteration when the bladder is involved. It is Wertheim operation with removal of the bladder and the ureters are implanted into the sigmoid colon (uretero-colic anastomosis) or into the rectum or into an ileal loop opening on the abdominal wall (ileal conduit).
 - ii. Posterior pelvic exenteration when the rectum is involved. It is Wertheim operation plus removal of the rectum and colostomy is performed.
 - iii. Total pelvic exenteration when the bladder and rectum are involved. It is Wertheim operation with removal of both bladder and rectum. Colostomy is performed and the ureters are implanted into the colon (wet colostomy) or into an ileal loop.
- Pelvic exenteration is applied in absence of extra-pelvic metastases. The primary mortality rate is 3-5%.

- b. Implantation of ureters into the sigmoid colon, rectum or an ileal loop in case of vesicovaginal fistula. Colostomy for rectovaginal fistula.
- c. The use of laser, diathermy coagulation or cryocautery for fungating masses and local recurrences.

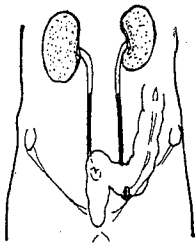


Fig.86. Ureterocolic implantation

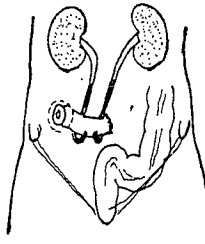


Fig.87. Ileal bladder

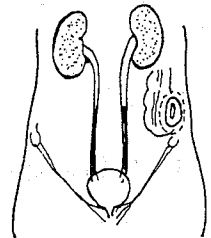


Fig.88. Colostomy

3. Medical Treatment

- a. Chemotherapy. As cisplatin, which is the most effective cytotoxic agent in cervical cancer. It is used when recurrence cannot be managed by radiation or surgery.
- b. Drugs to relieve pain as pethidine and morphine. Pain resulting from involvement of bone may respond to antiprostaglandin preparations as naproxen.
- c. Anabolic drugs and euphorants as amphetamine.
- d. Biological agents. Retinoids inhibit cell growth and induce differentiation. Immunological agents as interferons which inhibit cell growth. These drugs are under trials.

Treatment of carcinoma of cervix with pregnancy. See Obstetrics.

SUMMARY OF TREATMENT

1. Stage IA1: Simple hysterectomy or conization.
2. Stage IA2: Extended hysterectomy.
3. Stage IB and IIA: Wertheim operation or radiotherapy. The treatment is individualized e.g. if the patient is young surgery is preferred to preserve ovarian function and allow normal intercourse, as radiotherapy destroys ovarian function and causes vaginal stenosis and dyspareunia.
4. Stage IIB: Radiotherapy.
5. Stage III: Radiotherapy.
6. Stage IV: Palliative treatment including palliative radiotherapy, pelvic exenteration, chemotherapy and drugs to relieve pain.

Prognosis

The 5-year survival rate is as follows:

- | | |
|---------------------------------|--------|
| - Microinvasive carcinoma (IA): | 99% |
| - Stage IB: | 80-90% |
| - Stage II: | 60-70% |
| - Stage III: | 30-40% |
| - Stage IV: | 0-20% |

The main factors which affect prognosis are extent of the tumour, size of the tumour, and lymph node involvement.

STUMP CARCINOMA

Sometimes, carcinoma starts in the stump of the cervix left after subtotal hysterectomy. The incidence is about 1-10%. True stump carcinoma appears 2 years or more after subtotal hysterectomy while coincidental stump carcinoma appears within 2 years after the operation and indicates that the lesion was present but missed at the time of subtotal hysterectomy. The prognosis is bad because the bladder and rectum are found at the top of the stump and so, they become invaded early. Treated by surgery or irradiation. However, surgery is difficult because the anatomy is disturbed. Surgery includes radical removal of the tumour, with removal of the upper part of the vagina and pelvic lymph nodes. Radiotherapy is not satisfactory because the bladder and rectum are near and limit the dose of radium and the incidence of fistula is high, however, radiotherapy is the treatment of choice. The 5-year survival rate is 30-60%.

THE DIFFERENTIAL DIAGNOSIS OF CERVICAL CARCINOMA

A. ULCERATIVE LESIONS

1. **Cervical erosion.** It is bright red in colour while carcinoma is usually dark red. There is no induration, friability or necrosis. If there is any doubt we take a cervical smear or examine with colposcope.
2. **Infected cervical laceration.** History of recent abortion; labour or operation on the cervix. There is no induration, friability or necrosis.
3. **Trophic ulcer in case of prolapse.** There is no induration, friability or necrosis. Uterine prolapse is very rare with carcinoma of cervix because infiltration of parametrium fixes the uterus preventing its descent.
4. **Bilharzial ulcer.** The patient is young with a history of bilharziasis as terminal haematuria. There is no induration, friability, or necrosis. Bilharzial ova can be shown by colposcopy, cervical smear or by scraping the lesion. Biopsy is done to confirm the diagnosis.
5. **Tuberculous ulcer.** It is single or multiple with a serpiginous outline, undermined edge and yellow floor. It is soft in consistency, there is no induration, friability or necrosis. In the majority of cases, the ulcer is secondary to a tuberculous lesion elsewhere in the body. Biopsy confirms the diagnosis.
6. **Chancre of the cervix.** The ulcer is round with sharp edge. The material obtained from the lesion is examined by dark-ground illumination to detect spirochetes. Serological tests for syphilis start to be positive 2 weeks after appearance of the chancre.
7. **Herpetic ulcers.** See genital herpes.

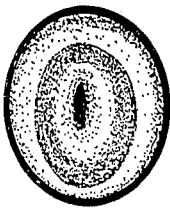


Fig.89. Cervical erosion



Fig.90. Tuberculous ulcer

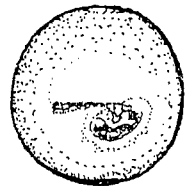


Fig.91. Chancre

B. PROLIFERATIVE LESIONS

1. **Adenomatous (mucous) polyp.** It appears as one or more soft swellings projecting from the external os, it may bleed on touch but it is not indurated or friable. Every cervical polyp should be removed and examined microscopically to exclude malignancy.
2. **Fibroid polyp.** This may distend the cervical canal and appears at the external os. It has a pedicle attached to the body or cervix but the cervical canal is free and smooth.

3. **Bilharzial polypi.** The patient is young with a history of bilharziasis as terminal haematuria. It is usually multiple, no induration, friability or necrosis. Biopsy confirms the diagnosis.
4. **Tuberculous polypi.**
5. **Condylomata acuminata.**
6. **Endometriosis of the cervix.**
7. **Grape-like sarcoma "sarcoma botryoides".** This tumour arises in the cervix or vagina. It mostly occurs in infants and young children. It forms a mass of soft polypi like a bunch of grapes, it grows rapidly and may even appear at the vulva. Highly malignant and fatal within 1-2 years if not treated.

C. ENDOCERVICAL CARCINOMA

1. **Chronic hypertrophic cervicitis.** The cervix is enlarged, congested and firm due to excessive fibrosis. There is no friability or bleeding on passing a sound into the cervical canal.
2. **Interstitial cervical fibroid.** It causes diffuse enlargement of the cervix. There is no friability or bleeding on passing a sound into the cervical canal. Sonography is helpful.
3. **Retained products of conception.** As a result of incomplete abortion, there may be a friable bleeding mass in the cervical canal, the mass is not fixed to the cervix and after removal with a ring forceps the cervix is found normal.
4. **Other causes** of bleeding higher up in the genital tract as cancer of body or senile endometritis because the cervix may look normal in early cases of endocervical carcinoma.

NEOPLASMS OF THE CORPUS UTERI

I. Benign:

- Leiomyoma (myoma, fibroid)
- Rare tumours as haemangioma, chondroma and osteoma.

II. Malignant:

A. Primary:

- Carcinoma.
- Sarcoma.
- Choriocarcinoma.
- Mixed mesodermal tumours. The tumour is a carcinosarcoma.

B. Secondary.

LEIOMYOMA OF THE UTERUS (MYOMA, FIBROID)

DEFINITION

Leiomyoma is a benign neoplasm arising from smooth muscle fibres. However, the tumour contains connective tissue fibres as well and so it is also called myofibroma or fibromyoma. Fibroid is the commonest term.

PATHOLOGY

Prevalence. About 20% of women above the age of 35 have fibroids. Excluding pregnancy, fibroid is the commonest pelvic tumour.

Age. The commonest age incidence is between 35-45 years.

Parity. More common in nulliparae and women with low parity.

Race. More common in black women.

Genetic factor. There is a familial tendency to develop fibroids. Certain genes on chromosomes 7 and 12 are related to the pathogenesis of fibroids.

Aetiology. The exact aetiology is unknown, however, the tumour is oestrogen dependent and excessive oestrogen stimulation predisposes to fibroids and this is evidenced by: (1) fibroids never start before puberty or after menopause and existing tumours usually undergo atrophy after the menopause; (2) they are frequently associated with other lesions caused by excessive oestrogen as endometrial hyperplasia, endometriosis and endometrial carcinoma; (3) they are more common in nulliparae because the high progesterone level during pregnancy antagonises oestrogen; (4) the tumour has more oestrogen receptors compared with the normal

surrounding myometrium; (5) anovulation may lead to development of fibroids as oestrogen is not opposed by progesterone.

Site of origin. (a) The body of uterus in about 97% of cases; (b) the cervix in about 3% of cases; (c) rare sites include the round ligament, uterosacral ligament and from the smooth muscle fibres between the 2 layers of the broad ligament.

Size. It varies from very small fibroids (seedlings) to huge tumours filling the whole abdomen.

Shape. The fibroid starts as a small spherical tumour but as it enlarges its shape may be changed by compression.

Types. Fibroids in the uterine body may be interstitial (intramural), subserous or submucous. The interstitial fibroid remains in the myometrium, the subserous lies beneath the peritoneum and the submucous is covered with endometrium. As a result of uterine contractions a submucous fibroid may bulge into the uterine cavity and develops a pedicle to form a polyp.

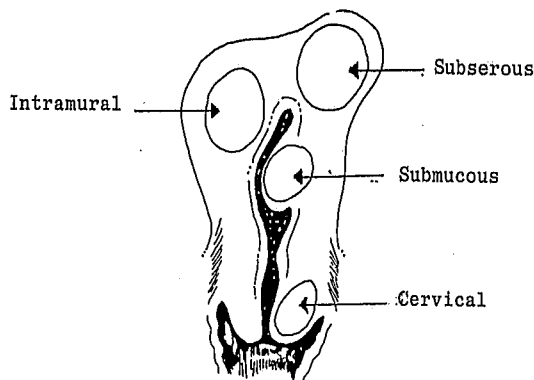


Fig.92. Sites of uterine myomas

Consistency. Firm unless affected by degeneration. The tumour becomes soft during pregnancy or due to hyaline or cystic degeneration. It is hard when calcified.

Macroscopic appearance. The tumour is white in colour because it is poor in blood supply. The cut surface shows a whorled appearance due to interlacing of muscle and connective tissue fibres. The interstitial fibroid is surrounded by a false capsule made of compressed uterine muscle. The capsule contains blood vessels which supply the tumour and it is the source of bleeding during myomectomy.

Microscopic appearance. The tumour is composed of smooth muscle fibres in a connective tissue stroma. The nucleus of the muscle cell is thick, short with rounded ends. The nucleus of the fibroblast is thin and filiform. By the Van Gieson stain, the muscle fibres appear yellow and the connective tissue fibres appear red.

Blood supply of fibroids. (1) Interstitial fibroid receives blood vessels from the surrounding capsule, the vessels pass radially towards the centre of the tumour and so if calcification occurs it starts at the periphery of the tumour as calcium is deposited from blood, also hyaline degeneration always starts at the centre of the tumour which is poor in blood supply; (2) subserous fibroid receives blood vessels from the pedicle because the peritoneal coat is not vascular; (3) submucous fibroid receives blood vessels from the pedicle and from the covering endometrium.

Rate of growth. Fibroids grow slowly at a rate of about one inch per year.

EFFECT OF FIBROIDS ON PELVIC ORGANS

- A. **The uterus.** (1) Vascularity is increased, the blood vessels are dilated and may become varicosed; (2) the myometrium is hypertrophied and thickened; (3) the endometrium is usually thickened, hyperplastic, very vascular and may show polypi; (4) the uterine cavity becomes enlarged with submucous and interstitial fibroids leading to increase in the surface area of endometrium; (5) position: The uterus may be displaced forwards, backwards, upwards (cervical fibroid) or laterally by the tumour; (6) a submucous fibroid or a fibroid polyp in the region of the fundus may cause chronic inversion of uterus.
- B. **Tubes and ovaries.** In about 15% of cases the tubes show evidence of chronic salpingitis in the form of hydrosalpinx, pyosalpinx or peritubal adhesions. The tube becomes elongated and stretched with a large broad ligament tumour. In about 20% of cases the ovaries are cystic showing follicular cysts and the tunica albuginea may be thickened.
- C. **Changes in urinary tract.** (1) A large broad ligament or cervical fibroid compresses the ureter leading to hydronephrosis and hydronephrosis; (2) pressure on the bladder causes frequency of micturition; (3) the urethra may become stretched by a cervical fibroid causing dysuria or retention of urine.
- D. **Rectum.** A posterior cervical myoma may compress the rectum leading to constipation and piles.

SECONDARY CHANGES IN FIBROIDS

- (1) Atrophy; (2) necrosis; (3) degeneration;
(4) infection; (5) vascular changes; (6) malignancy.

1. Atrophy

It normally occurs after menopause, natural or artificial, due to lack of oestrogen and reduced blood supply to the uterus.

2. Necrosis

Due to complete cutting of the blood supply of the tumour leading to death of tissue. Necrosis may occur after torsion of a subserous fibroid or application of intracavitary radium.

3. Degeneration

- a. **Hyaline degeneration.** It is the commonest degeneration. It usually starts at the centre of a large tumour because it is the least vascular area. The affected area is replaced by hyaline material and appears structureless, homogeneous and loses its whorled appearance. Clinically, the patient may complain of dull aching pain and the tumour becomes soft in consistency. Sometimes, the hyaline material liquefies forming cystic spaces filled with colourless or blood stained fluid.
- b. **Cystic degeneration.** It is the result of liquefaction of hyaline material leading to the formation of cystic spaces. The condition may also follow red degeneration, dilatation of blood vessels (telangiectasis) or lymphatics (lymphangiectasis). Clinically, the tumour becomes soft or cystic in consistency and may be mistaken for a pregnant uterus.
- c. **Fatty degeneration.** Fat globules are deposited inside the muscle fibres or in between the fibres (fatty infiltration). The tumour becomes soft in consistency and yellow in colour.
- d. **Calcification (calcareous degeneration).** It is usually preceded by fatty degeneration. It occurs in tumours with poor blood supply and so it usually occurs after menopause and in subserous fibroids. Calcium salts (carbonate or phosphate) are deposited from the blood and so calcification is found at the periphery of the tumour and along the blood vessels passing radially towards its centre. Sometimes, the whole tumour becomes calcified (womb stone). Clinically, the tumour becomes stony hard in consistency and gives a characteristic X-ray shadow (honeycomb like calcification).
- e. **Red degeneration (necrobiosis).** It may occur during pregnancy (usually in the second trimester), labour, puerperium and very rarely with combined contraceptive tablets and in postmenopausal women receiving oestrogen replacement therapy. It is incomplete necrosis from which the tissues can recover. It affects interstitial fibroids.

Pathology. The tumour becomes soft, red in colour (salmon pink) and may give a fishy odour due to secondary infection with *E. coli*. The staining is due to diffusion of haemoglobin pigment throughout the tumour. Microscopically, there is thrombosis in the blood vessels of the capsule. The colour darkens after exposure to air due to formation of methaemoglobin.

Aetiology. The true cause is unknown, but it is believed that thrombosis occurs in the blood vessels of the capsule leading to ischaemia and incomplete necrosis of the tumour. The ischaemic cells produce a lipid toxin which causes intravascular haemolysis, then haemoglobin diffuses out of the blood vessels staining the tumour red. The condition is more common during pregnancy due to (a) increased fibrinogen and other clotting factors (7, 8, 9, 10) favouring thrombosis; (b) rapid growth of uterus leads to kinking of the blood vessels of the capsule and this favours thrombosis; (c) increased vascularity of uterus leading to congestion, stasis and thrombosis.

Clinical Picture. Sudden onset of severe abdominal pain localized over the affected tumour and may be accompanied with vomiting. Mild fever usually occurs after some hours due to

absorption of haemoglobin. On palpation the tumour is very tender. Sometimes, the condition is subacute with mild symptoms.

Treatment: Medical by rest in bed, and analgesics for pain. Surgical treatment is indicated if medical treatment fails or if we are not sure of the diagnosis, laparotomy is done and only the affected tumour is removed (known by adherent omentum).

4. Infection

This may occur in the following conditions: (a) fibroid polyp usually becomes ulcerated and infected at its lower pole due to poor blood supply; (b) submucous fibroid may become infected after abortion, labour, curettage or application of radium; (c) subserous fibroid may become infected from a neighbouring organ as bowel or appendix; (d) infection may follow red degeneration; (e) infection from the bloodstream which is rare.

5. Vascular changes

(a) Oedema and this is common during pregnancy and also occurs when the tumour becomes impacted in the pelvis; (b) congestion due to torsion of a subserous fibroid; (c) telangiectasis; (d) lymphangiectasis usually due to severe oedema.

6. Malignancy

Change into sarcoma is rare and occurs in 1 to 5 per thousand cases. It is a leiomyosarcoma or fibrosarcoma. The affected area loses the whorled appearance; it becomes soft and yellow in colour with areas of haemorrhage and necrosis. Malignancy is suspected in the following conditions: (a) rapid growth of the tumour; (b) growth of the tumour after menopause; (c) postmenopausal bleeding; (d) the tumour becomes painful and tender; (e) recurrence of a fibroid polyp after its removal; (f) loss of weight and cachexia; (g) evidence of distant metastases, e.g. in the lung or liver.

DIAGNOSIS

I. Symptoms

In about 50% of cases the condition is symptomless and discovered accidentally, however, the patient may complain of one or more of the following:

1. Abnormal Uterine Bleeding

This may be in the form of menorrhagia, polymenorrhoea or metrorrhagia.

Menorrhagia. The commonest symptom and is caused by: (a) increased vascularity of the uterus; (b) endometrial hyperplasia; (c) increase in the surface area of the endometrium due to enlargement of the uterine cavity; (d) the presence of fibroids mechanically interferes with uterine contractions which help to stop the bleeding; (e) associated anovulation.

Polymenorrhoea. It is due to ovarian congestion which is a part of pelvic congestion caused by the presence of fibroids. Ovarian congestion causes early degeneration of the corpus luteum.

Metrorrhagia. It is due to: (a) ulceration of a submucous fibroid or a fibroid polyp; (b) malignant change in the fibroid; (c) associated lesions as endometrial polypi, endometrial carcinoma and dysfunctional uterine bleeding.

2. Vaginal Discharge

(a) Watery discharge due to pelvic congestion and increased surface area of the endometrium; (b) purulent or blood stained discharge due to ulceration and infection of a fibroid polyp.

3. Pain

This may be in the form of: (a) congestive dysmenorrhoea; (b) colicky pain caused by uterine contractions to expel a fibroid polyp; (c) lower abdominal pain and heaviness caused by large tumours; (d) pain due to complication for example red degeneration or torsion of a subserous fibroid causes acute abdominal pain; hyaline degeneration causes dull aching pain, infection causes pain and fever, also pain may be caused by malignant change; (e) pain due to associated lesions as salpingitis or endometriosis.

4. Infertility

Present in about 30% of cases and may be caused by: (a) mechanical obstruction by a cervical fibroid (cervical factor); (b) a submucous fibroid may prevent implantation of the ovum or causes early abortion (uterine factor); (c) blocked tubes by cornual fibroids, broad ligament tumour or associated salpingitis (tubal factor); (d) anovulation due to thickened tunica albuginea (ovarian factor); (e) increased distance for sperm to travel. About 40% of women will conceive after myomectomy. However, all other causes of infertility should be excluded before deciding that the myoma is the cause.

5. Abdominal Mass

This may be the only complaint particularly with a large subserous fibroid.

6. Pressure Symptoms

These are more liable to occur with a cervical fibroid which may cause renal colic, frequency of micturition, dysuria, acute retention or chronic retention with overflow. Pressure on the rectum leads to constipation and piles. Also a large abdominal tumour may cause dyspnoea and palpitation.

7. Symptoms during Pregnancy

As abortion and preterm labour.

8. General Symptoms

Symptoms of anaemia as headache and palpitation if there is excessive blood loss.

Symptoms of polycythaemia which is a rare finding. It is usually caused by a large myoma in the broad ligament. The explanation is unknown but the tumour may compress the ureter and affect the erythropoietic function of the kidney or the tumour itself produces erythropoietin.

Hypoglycaemia is a very rare finding, likely to occur if the tumour is retroperitoneal causing pancreatic stimulation.

II. Signs

A. General Examination

Signs of anaemia if there is excessive bleeding.

B. Abdominal Examination

If the tumour is more than the size of 12 weeks pregnancy, it will give rise to a pelvi-abdominal mass. If less than the size of 12 weeks pregnancy, it will give rise to a pelvic mass.

1. Abdominal Tumours

There is a pelvi-abdominal swelling. Typically, it is irregular or knobby due to the presence of multiple fibroids. It is firm in consistency, mobile and not tender. It is dull on percussion and a uterine soufflé may be heard due to increased vascularity of the uterus. Vaginally, the swelling is continuous with the uterus and moves with movement of the cervix. If a uterine sound is introduced, it will show enlargement of the uterine cavity in case of submucous and interstitial fibroids.

2. Pelvic Tumours

Bimanual examination shows that the uterus is enlarged and firm. The enlargement may be symmetrical or asymmetrical in the presence of multiple fibroids. A pedunculated subserous fibroid may be mistaken for an ovarian tumour. A broad ligament fibroid is felt on one side of the uterus and displacing it laterally to the other side. A cervical fibroid is felt as a fixed firm swelling with the uterus on its top. With speculum examination a fibroid polyp may be seen coming from the cervical canal.

III. Investigations

1. Pelvic ultrasonography (either transabdominal or trans-vaginal). This shows the size, site and number of fibroids and differentiates the tumour from other swellings as ovarian tumour. Saline infusion sonography (hydrosonography), where saline is injected into the uterus during ultrasound allows better detection of a submucous myoma.
2. Hysterosalpingography (HSG). If infertility is a complaint, all investigations of infertility including



Fig.93. Filling defect seen in hysterosalpinogram

HSG are carried out to detect another cause of infertility. HSG confirms tubal patency and may reveal a submucous fibroid or a small fibroid polyp which appears as a filling defect.

3. Hysteroscopy may be used to diagnose a submucous fibroid or a small fibroid polyp.
4. Endometrial biopsy or uterine curettage is done if there is irregular uterine bleeding to exclude associated endometrial carcinoma.
5. Intravenous pyelogram is done in cases of cervical and broad ligament fibroid to show the course of ureter, to diagnose hydroureter and hydronephrosis and to assess kidney function.
6. CT scan or magnetic resonance imaging may be helpful in difficult cases when ultrasound cannot differentiate between myoma and localized adenomyosis and between broad ligament fibroid and ovarian tumour.
7. Other investigations to prepare the patient for operation.

DIFFERENTIAL DIAGNOSIS

1. Causes of a pelvi-abdominal swelling as ovarian tumour.
2. Causes of symmetrically enlarged uterus as diffuse adenomyosis.
3. Fibroid polyp is to be differentiated from any mass protruding from the cervix as chronic inversion of uterus.
4. A broad ligament fibroid may be confused with a broad ligament cyst or a tubal mass as hydro- or pyosalpinx.
5. Posterior wall fibroid has to be differentiated from other masses felt in Douglas pouch.

COMPLICATIONS OF FIBROIDS

1. Menorrhagia which leads to anaemia.
2. Torsion of a pedunculated subserous fibroid leads to acute abdominal pain.
3. Rupture of a vein on the surface of a subserous fibroid leads to internal haemorrhage.
4. Infection of the tumour.
5. Degenerative changes as hyaline and red degeneration.
6. Malignant change.
7. Inversion of uterus caused by a fundal submucous fibroid or fibroid polyp.
8. Infertility.
9. Uterine prolapse. Small fibroids increase the weight of the uterus also a large cervical fibroid polyp applies traction on the uterus.
10. Ascites and pseudo-Meigs syndrome. Pedunculated subserous tumour can cause ascites, possibly by mechanical irritation of the peritoneum. Rarely the ascites is accompanied by hydrothorax, mostly on the right side, to produce a pseudo-Meigs syndrome.
11. Complications during pregnancy. There is increased incidence of abortion, incarceration of a retroverted gravid uterus, preterm labour, pressure symptoms, malpresentation, nonengagement of the presenting part, ectopic pregnancy, and placenta praevia.

12. Complications during labour. Obstructed labour, prolonged labour, retained placenta, and postpartum haemorrhage.
13. Complication during the puerperium. Subinvolution of uterus, secondary postpartum haemorrhage and puerperal sepsis.

TREATMENT

1. No Treatment

Small symptomless fibroids require no treatment but the patient is kept under observation and examined clinically and by ultrasound every 6 months. The exceptions to this rule are:

- a. If the size of the tumour is more than 12 weeks pregnancy. This is a matter of controversy.
- b. Pedunculated subserous fibroid which is liable to torsion.
- c. If the tumour is growing rapidly.
- d. Growth after menopause.

2. Medical Treatment

If for any reason the operation has to be postponed, menorrhagia is temporarily controlled by a progestogen (Provera tablets or Depo-Provera IM), antiprostaglandin, tranexamic acid, danazol, gestrinone, or a gonadotrophin releasing hormone analogue (agonist). The latter is given for three months. It leads to amenorrhoea and reduction of tumour size by 25-50%. This makes subsequent operation easier and with less blood loss. Mifepristone can be given in a dose of 50 mg/day for 3-6 months. It reduces the size of myomas by 50%. Mirena coil treats menorrhagia, and reduces the size of fibroids.

3. Surgical Treatment

It is indicated for large or symptomatic tumours. Myomectomy, hysterectomy, or myolysis is performed.

A. Myomectomy

It means removal of fibroids from the uterus leaving behind the organ to carry its function which is menstruation and pregnancy.

Indications

(1) It is the operation of choice in all women below the age of 40 who want to become pregnant; (2) a small fibroid polyp not larger than 8 weeks pregnancy is removed by vaginal myomectomy; (3) a submucous fibroid less than 5 cm in diameter is removed using the hysteroscope.

Contraindications

(1) If the patient is above the age of 40; (2) blocked tubes as bilateral hydrosalpinx or pyosalpinx because it is useless to leave behind the uterus as the patient will be sterile, unless IVF and ET is planned for; (3) multiple fibroids if it is found that the operation will leave

behind a useless organ; (4) cervical fibroid is usually treated by hysterectomy; (5) if malignancy is suspected; (6) the presence of other lesions in the uterus as adenomyosis.

Note. A written consent for hysterectomy should be obtained from the patient and husband before myomectomy as hysterectomy may be needed during the operation.

B. Hysterectomy

Indicated when myomectomy is contraindicated. Total hysterectomy is performed to avoid stump carcinoma. If the patient is 50 years or above, we remove both ovaries, even if they are healthy because they are potentially malignant.

C. Myolysis

Using the laparoscope a needle is inserted into the myoma to destroy it by burning or freezing (cryotherapy). These methods lead to necrosis and shrinkage of the tumour. Excessive intra-abdominal adhesions and uterine rupture during pregnancy have been reported. Indicated when patient is unfit for hysterectomy or refuses it.

4. Embolization of Both Uterine Arteries

The tumour size is reduced by about 50%. It may be complicated by uterine infection in the form of endometritis and pyometra as well as infection of the necrotic fibroids. Indicated when patient is unfit for hysterectomy or refuses it. For angiographic embolization, a local anaesthesia is given and a catheter is passed along the femoral artery to reach the aorta. A radio-opaque dye is injected to show the pelvic arteries. A catheter is then passed to block the uterine artery on both sides using small pieces (2 x 2 x 2 mm) of Gelfoam or other material.

SPECIAL TYPES OF FIBROIDS

A. Cervical Fibroid

The neoplasm arises from the smooth muscle fibres of the cervix. It accounts for about 3% of all fibroids and is usually single.

Types

1. Fibroid arising in the supravaginal portion of the cervix. It remains interstitial and causes displacement and compression of one or both ureters.
2. Fibroid arising in the portio vaginalis of the cervix. It remains interstitial causing barrel-shaped enlargement of the cervix or it forms a cervical polyp.

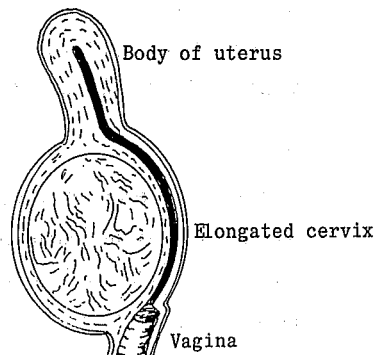


Fig. 94. Cervical fibroid

Symptoms

1. Pressure symptoms. These may take the form of renal colic, frequency of micturition, dysuria or acute retention of urine as the cervical fibroid stretches the urethra and interferes with the opening of the internal urethral sphincter. Retention usually occurs few days before menstruation due to premenstrual pelvic congestion which causes enlargement of the fibroid. Pressure on the rectum leads to constipation and piles.
2. Infertility due to obstruction of the cervical canal.
3. Vaginal discharge due to ulceration and infection of a fibroid polyp.
4. Dyspareunia caused by a large cervical polyp.

Note. Cervical fibroid does not cause menorrhagia because the cervical mucosa does not shed during menstruation.

Signs

1. A large interstitial cervical fibroid is felt as a firm fixed pelvic mass with the uterus lying on its top.
2. The tumour arising in the portio vaginalis causes barrel-shaped enlargement of the cervix or forms a cervical polyp.

Treatment

1. The interstitial cervical fibroid is usually treated by abdominal hysterectomy as myomectomy is difficult (difficult to control bleeding and to obliterate the dead space left after myomectomy). Before operation, an intravenous pyelogram is done to show the course of the ureters and assess kidney function.
2. A cervical fibroid polyp is removed by vaginal polypectomy (myomectomy).

B. Fibroid Polyp

See uterine polypi.

C. Parasitic Fibroid

The condition occurs when a pedunculated subserous fibroid undergoes torsion and forms adhesions with the omentum and other structures. The tumour acquires a new blood supply from these structures and becomes completely detached from the uterus and forms a free intra-abdominal mass.

D. Intravenous Leiomyomatosis

It is a very rare lesion in which smooth muscle cells are found in the pelvic veins. The tumour either extends from adjacent myoma in the uterus or arises from the smooth muscle wall of uterine veins. It may metastasize to the lung or to other sites.

E. Leiomyoma Peritonealis Disseminata

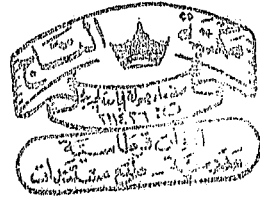
Benign myomatous nodules are found on the peritoneal surfaces and in the omentum. Most commonly associated with pregnancy or high oestrogen states.

ENDOMETRIAL HYPERPLASIA

It is due to prolonged periods of oestrogenic stimulation of the endometrium which is unopposed by progesterone i.e. anovulatory cycles.

CONDITIONS ASSOCIATED WITH ENDOMETRIAL HYPERPLASIA

1. Metropathia haemorrhagica.
2. In the years immediately following the menarche.
3. In the years prior to menopause.
4. Polycystic ovary syndrome.
5. Oestrogen producing ovarian tumours.
6. Oestrogen replacement therapy.
7. Obesity, especially in postmenopausal women, due to increased peripheral conversion of androstenedione to oestrone in body fat.
8. Tamoxifen therapy; when given to treat breast carcinoma for more than 5 years, increases the risk of endometrial hyperplasia, polypi, and carcinoma.



CLASSIFICATION

Endometrial hyperplasia is classified into:

1. Simple hyperplasia. Previously called cystic glandular hyperplasia. The glands are increased in number and become cystic. There is a variation in the size of the glands giving a "Swiss cheese" appearance. It progresses to malignancy in about 1% of cases.
2. Complex hyperplasia. Previously designated adenomatous hyperplasia. The glands are increased in number and crowded with little or no intervening stroma. Malignant change occurs in about 3% of cases.
3. Atypical hyperplasia. It includes simple hyperplasia with atypia and complex hyperplasia with atypia. The nuclei show atypia. They are irregular in shape and size, with dense chromatin clumping and large nucleoli with increased nuclear to cytoplasmic ratio. Progression to carcinoma occurs in about 10% of cases with atypical simple hyperplasia, and in 30% of patients with atypical complex hyperplasia.

DIAGNOSIS

The lesion leads to menorrhagia, irregular uterine bleeding, or postmenopausal bleeding. The uterus may be slightly enlarged and soft as in case of metropathia haemorrhagica due to high oestrogen level causing increased vascularity and hypertrophy of the myometrium. Diagnosis is made by uterine curettage and histopathological examination of the endometrium.

TREATMENT

It depends upon the age of the patient and type of endometrial hyperplasia.

A. Simple and Complex Hyperplasia (no atypia)

1. Young women: Treated conservatively by a progestogen, a progestogen releasing intra-uterine device (Mirena), a combined oral contraceptive, danazol or gonadotrophin releasing hormone analogue. These lead to endometrial atrophy. Progestogens are given on cyclic basis e.g. norethisterone (Primolut-N) tablets in a dose of 10 mg daily (2 tablets) for 10 days each month for 3-12 months. Endometrial biopsy is done every 3 months to see response to treatment. In case of infertility ovulatory drugs as Clomid are given. Relapse may occur when therapy is stopped.
2. Women above 40 years: We give the same conservative treatment.
3. Postmenopausal patient: Hysterectomy is indicated for any type of endometrial hyperplasia.

B. Atypical Hyperplasia

1. Young woman: Treated conservatively as above. However, if a progestogen is used, it is given continuously and in a larger dose, e.g., 20 mg of norethisterone daily.
2. Women above 40 years: Hysterectomy is indicated.
3. Postmenopausal patient: Hysterectomy is done.

ENDOMETRIAL CARCINOMA

PATHOLOGY

Incidence. It varies between 20-30 per 100,000 females per year. This increases to 50 at the age of 50 years and increases thereafter. Nowadays there is increase in the incidence of endometrial carcinoma due to increased longevity, increased use of oestrogen in the treatment of menopausal symptoms, and better methods of diagnosis. At the same time there is a decrease in the frequency of invasive cervical carcinoma due to the routine screening by the cervical smear which helps to detect and treat precancerous lesions of the cervix. In the United States and other western countries, endometrial carcinoma is more prevalent than cervical carcinoma and is the most common malignancy of the female genital tract accounting for about 50% of cases. In eastern countries, cervical carcinoma is more common than endometrial carcinoma.

Age. The commonest age incidence is 55-70 years. Seventy-five percent of cases occur after the menopause. The relative infrequency before the menopause (25%) may be related in part to the monthly shedding of the endometrium.

Parity. More common in nulliparae and women with low parity.

Social and economic state. More common among the higher classes.

Race. More common in Jewish women and in white women more than in black women.

Aetiology. The cause of endometrial carcinoma is unknown, but the following are predisposing factors:

1. **Hyperoestrogenism.** The disease is more common in women with early menarche before the age of 12 years, delayed menopause after the age of 52 years, infertility and those given prolonged oestrogen therapy. The disease is frequently associated with other lesions caused by excessive oestrogen as endometrial hyperplasia, endometriosis and fibroids. Endometrial carcinoma may also occur in association with oestrogenic ovarian tumours and polycystic ovary syndrome (unopposed endogenous oestrogen). Oestrone (E1) plays the main role as it is the major circulating oestrogen after the menopause.
2. **Diabetes mellitus.** The disease is more common in diabetics and women with impaired glucose tolerance (10-30% are diabetics). Hyperinsulinaemia may increase the risk by increasing insulin growth factor I activity in the endometrium.
3. **Obesity.** Androstenedione (weak androgen produced by ovaries and adrenal glands) is converted to oestrone in body fat. The rate of conversion is increased in the obese, the diabetic and after menopause. Also oestrogen is stored in fat leading to a prolonged action on the endometrium.
4. **Hypertension.** However, hypertension, is common in this age group and is not more common in association with this type of cancer. The association of diabetes, obesity and hypertension in a patient with endometrial carcinoma is referred to as the corpus cancer syndrome.
5. **Senile endometritis and pyometra** (causing chronic irritation).
6. **Genetic factor.** There is a familial tendency to develop endometrial carcinoma. Also women with breast cancer or Lynch II syndrome have increased risk of developing E.C.
7. **Tamoxifen therapy;** when given to treat breast carcinoma for more than 5 years increases the risk of endometrial hyperplasia, polypi, and carcinoma.
8. **Chronic liver disease.** Oestrogen is metabolised in the liver, and its level is increased in liver disease.
9. **Previous pelvic radiotherapy,** e.g. for cervical carcinoma.

Precancerous Lesions

1. Simple endometrial hyperplasia progresses to malignancy in about 1% of cases.
2. Complex hyperplasia progresses to malignancy in about 3% of cases.
3. Atypical hyperplasia becomes malignant in about 10% of cases with atypical simple hyperplasia and in 30% of patients with atypical complex hyperplasia.

Macroscopic Appearance

1. **Localized type.** The tumour appears as a localized mass which may become polypoidal.
2. **Diffuse type.** A great part of the endometrium undergoes malignant change.

Endometrial carcinoma usually arises in the fundus and tends to remain localized.

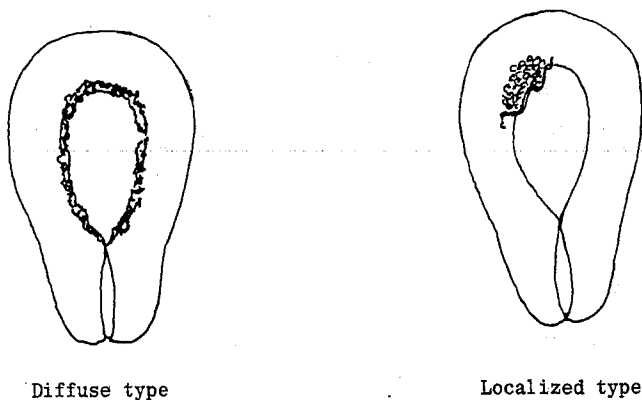


Fig.95. Endometrial carcinoma

Microscopic Appearance

1. Adenocarcinoma; found in the great majority of cases (90%).
2. Papillary serous adenocarcinoma.
3. Clear cell adenocarcinoma which resembles renal clear cell carcinoma.
4. Squamous cell carcinoma, found in occasional cases due to metaplasia of columnar epithelium into squamous epithelium as in case of senile endometritis and pyometra.
5. Adenoacanthoma. It is an adenocarcinoma with areas showing benign squamous epithelium. These areas form more than 10% of the tumour.
6. Adenosquamous carcinoma. It is a mixed columnar and squamous cell carcinoma.
7. Carcinosarcoma. It is adenocarcinoma with a malignant stroma, i.e. sarcomatous connective tissue stroma.
8. Small cell carcinoma.

MODE OF SPREAD

1. **Direct spread.** The tumour invades the myometrium slowly to reach the peritoneum leading to adhesions or even malignant fistula with the bladder or bowel. Extension to the cervix may cause cervical obstruction and pyometra. Endometrial carcinoma is considered as "surface rider" and may take several years to invade the surrounding structures. This is sometimes attributed to the presence of a barrier of polysaccharides in the endometrium.
2. **Lymphatic spread.** This occurs late in the disease. The pelvic lymph glands are involved in 10-30% of cases depending upon the stage of the disease. The nodes involved depend upon the site of the tumour. The upper third of the body including the fundus drains along the ovarian lymphatics into the para-aortic lymph nodes. The middle third drains mainly into the internal iliac glands. The lower third drains with the cervix. The cornua of uterus drain by lymphatics passing along the round ligaments into the inguinal lymph nodes. Local spread to the tubes and ovaries occurs by direct invasion as well as by lymphatics. Retrograde lymphatic or venous spread may lead to secondaries in the vagina or vulva.

3. **Bloodstream.** Spread by the bloodstream to distant organs as the liver, lungs, brain and bones occurs late when the disease is advanced.
4. **Surface implantation (seeding).** This may lead to appearance of secondaries in the vaginal vault after hysterectomy for endometrial carcinoma (10%). This is the commonest site for recurrence.

Note. The vagina and lungs are the common metastatic sites.

COMPLICATIONS

(1) Pyometra; (2) peritonitis, when the tumour perforates the wall of the uterus; (3) malignant fistula may develop into the bladder or bowel; (4) adhesions and intestinal obstruction; (5) ureteric obstruction and uraemia; (6) haemorrhage; (7) cachexia.

Diagnosis

The typical patient is a nulliparous, hypertensive, obese, diabetic, above the age of 50 years.

A. Symptoms

The patient may complain of one or more of the following:

1. **Vaginal bleeding.** It is the main symptom. It takes the form of menorrhagia, metrorrhagia, or postmenopausal bleeding. It is postmenopausal bleeding in more than 75% of cases. Prolonged blood loss leads to anaemia.
2. **Vaginal discharge.** It starts as a watery discharge due to mucus secretion of the malignant endometrial glands. Later on with ulceration and infection the discharge becomes blood stained and offensive and may contain necrotic debris. Occasionally the patient passes a piece of polypoid growth per vagina.
3. **Pain.** It is a late symptom, it is due to pyometra or involvement of the peritoneum, or extrauterine spread. Simpson pain is colicky pain felt in the suprapubic region, it appears at the same time each day and lasts for 1-2 hours. It is due to expulsive uterine contractions, and noted by 15% of patients.
4. **Cachexia.** It occurs in advanced cases. It is due to repeated blood loss, infection, toxic absorption, pain and loss of sleep.

B. Signs

1. **General examination.** This may show cachexia. The patient is usually hypertensive, obese, and diabetic. The left supraclavicular and inguinal lymph nodes are palpated for metastases. The lower limbs are examined for oedema which indicates obstruction of lymphatics in the pelvis.
2. **Abdominal examination.** As the tumour grows slowly, the uterus is usually not felt abdominally unless there is associated fibroids or pyometra. Ascites may be present if there is visceral or peritoneal involvement. The liver and kidneys are palpated.

3. Pelvic Examination:

- a. The tumour grows slowly and so the uterus is normal in size, or it may be smaller than normal if there is marked postmenopausal atrophy. However, the uterus may be enlarged by the tumour, by pyometra or by associated fibroids which are present in 30% of cases.
- b. Metastasis may be seen at the lower end of the anterior vaginal wall alongside the urethra (suburethral-paraurethral) and appears as a red swelling.
- c. Rectal examination must be done in every case to detect infiltration of uterosacral ligaments and spread to the rectum. The ligaments are better felt per rectum.
- d. Very rarely, pelvic or inguinal glands are clinically palpable.

C. Investigations

1. Transvaginal sonography. Endometrial carcinoma can be diagnosed by sonography. However, endometrial biopsy must be taken to confirm the diagnosis.
2. Cervical smear. Taken in absence of bleeding to detect the presence of malignant cells which may come from the cervix, endometrium, tubes or ovaries. It is positive in about 50% of cases of E.C.
3. Endometrial biopsy. It must be done in every woman above the age of 40 years complaining of abnormal uterine bleeding, as it is the only sure method to diagnose endometrial carcinoma. Endometrial biopsy is taken by one of three methods; fractional uterine curettage, endometrial aspiration, or hysteroscopy.
 - a. Fractional uterine curettage. Separate specimens are taken from the cervical canal and body of the uterus. It detects endocervical carcinoma and endometrial carcinoma which may be extending to the cervix. In case of endometrial carcinoma, the material obtained is plentiful, cheesy, pale yellow, necrotic and friable. Failure of the uterine wall to grate is suspicious (silent curettage). A blunt curette is used because the uterus is soft and easily perforated by a sharp curette. Small growths may be missed with the curettage. This happens in about 10% of cases.
 - b. Endometrial aspiration. The Vabra aspirator or Pipelle suction curette is used to obtain endometrial tissue by suction by creating a negative pressure. The advantages over uterine curettage are: (1) done without anaesthesia which may be contraindicated by the presence of marked obesity, hypertension, or diabetes mellitus; so it is done as an outpatient procedure; (2) less cost; (3) complications as perforation are less. Endometrial aspiration detects endometrial carcinoma in about 95% of cases, and has replaced uterine curettage for the diagnosis of endometrial carcinoma and postmenopausal bleeding.
 - c. The use of hysteroscope. It is the most reliable method for diagnosis. The hysteroscope inspects the uterine cavity and endocervix. It can show small tumours missed by curettage. It also allows inspection of the growth and determines its extent which helps in planning therapy. Hysteroscopy is followed by full uterine curettage or directed

endometrial biopsy from abnormal areas. It can be done without anaesthesia as an outpatient procedure (office hysteroscopy using a flexible hysteroscope).

4. Cystoscopy to diagnose infiltration of the bladder.
5. Sigmoidoscopy or barium enema if there are bowel symptoms as pain or bleeding.
6. Chest X-ray is done as a routine.
7. Intravenous pyelogram to assess kidney function and outline the course of the ureters. It must be done in every case.
8. Computerized tomography (CT) scan to the pelvis and abdomen. It shows the size of the tumour, infiltration of myometrium, extension to the cervix, metastases in pelvic and aortic lymph nodes and liver and diagnoses hydronephrosis.
9. Magnetic resonance imaging (MRI) is more accurate than CT scan but it is costly.
10. Bone scan. Done only when symptoms or signs suggest metastases.
11. Serum estimation of the tumour marker CA-125 (cancer antigen-125), to follow response to treatment and to detect recurrence.
12. Oestrogen and progesterone receptors are measured in tumour cells obtained by biopsy to detect the response to hormonal therapy if it is needed.
13. Laboratory tests: (a) Complete blood count; (b) urine analysis; (c) renal function tests; (d) liver function tests; (e) fasting blood sugar; (f) serum electrolytes.
14. Electrocardiogram.

Notes for the postgraduate

1. The findings of endometrial carcinoma on transvaginal sonography include; (1) increased endometrial thickness: more than 4 mm in postmenopausal women and more than 8 mm in perimenopausal women; (2) the presence of an echogenic mass in the endometrium; (3) loss of the subendometrial sonolucent layer indicates myometrial invasion. This layer is formed by the subendometrial blood vessels; (4) intrauterine fluid; (5) fluid in Douglas pouch. When the endometrial thickness is 4 mm or less, the possibility of endometrial carcinoma is rare.
2. With hysteroscopy, cancer cells can be pushed along the tubes to reach the peritoneal cavity (a drawback).
3. Smoking reduces the incidence of endometrial carcinoma, fibroids, and endometriosis by inducing a hypoestrogenic state through inhibition of the ovary and increasing androgen production from the adrenal glands.

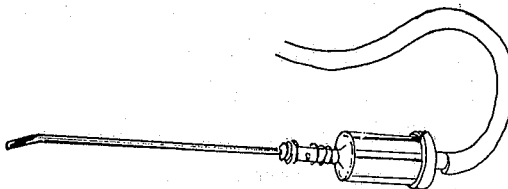


Fig.96. Vabra aspirator

DIFFERENTIAL DIAGNOSIS

1. All cases of peri- and postmenopausal bleeding. Endometrial biopsy must be done in these cases even there is a cause to explain the bleeding because this is the only way to exclude endometrial carcinoma.

2. In young patients it has to be differentiated from causes of irregular uterine bleeding as dysfunctional bleeding.
3. Causes of symmetrical enlargement of uterus.
4. Causes of pyometra.

FIGO STAGING (1988)

The stages are based on findings at operation.

Stage I: Tumour confined to the body of the uterus.

IA: Tumour limited to endometrium.

IB: Invasion up to or to less than half of the myometrium.

IC: Invasion to more than half of the myometrium.

Stage II: Tumour invades the cervix:

IIA: Involvement of endocervical glands only.

IIB: Invasion of cervical stroma.

Stage III:

IIIA: Tumour invades pelvic peritoneum and/or adnexa, and/or cancer cells in ascites or peritoneal washings.

IIIB: Direct extension to vagina or vaginal metastasis.

IIIC: Metastasis to pelvic and/or para-aortic lymph nodes.

Stage IV:

IVA: Tumour invades bladder and/or bowel mucosa.

IVB: Distant metastasis including intra-abdominal lymph nodes other than para-aortic and/or inguinal lymph nodes.

HISTOPATHOLOGY

E.C. is classified into 3 grades:

Grade1: Well differentiated tumour.

Grade2: Moderately differentiated tumour.

Grade3: Poorly differentiated tumour.

Note. Stage 0: Atypical endometrial hyperplasia but malignancy and invasion is not definite. Some call this lesion carcinoma in situ.

TREATMENT

Prophylactic Treatment

1. Oestrogen replacement therapy given to postmenopausal women should be combined with a progestogen given for 10-14 days every month to prevent endometrial hyperplasia and carcinoma.
2. Proper treatment of endometrial hyperplasia.
3. Endometrial biopsy should be done for every woman above the age of 40 years complaining of abnormal uterine bleeding to exclude endometrial carcinoma.

4. Cervical smear is done routinely to diagnose early cervical carcinoma. It detects endometrial carcinoma in about 50% of cases.
5. Postmenopausal women who have a high risk factor as late menopause (> 52 years), obesity, diabetes mellitus, and family history of endometrial carcinoma, are followed up by endometrial smear, endometrial biopsy, or endometrial aspiration, done every 1 to 2 years. The same follow-up is also done for women receiving tamoxifen therapy for breast carcinoma.

Treatment of Stage I

The treatment is total abdominal hysterectomy and bilateral salpingo-oophorectomy. To prevent spillage of cancer cells through the fallopian tubes, the tubes are clamped or ligated at the start of operation. Cervical closure and removal of the upper third of the vagina (vaginal cuff) with the uterus will not prevent subsequent metastases in the vaginal vault.

Postoperative external pelvic radiation or vaginal vault radiation using radium or caesium is given in the following conditions to reduce the incidence of pelvic recurrence:

1. The tumour invades beyond the inner third of the myometrium.
2. The tumour is grade 2 or 3 (moderately or poorly differentiated).
3. Lymph node involvement.

The results of radiotherapy alone are inferior to surgery. It is given if the patient is not fit for surgery. The whole uterine cavity and vaginal vault are packed with radium or caesium. This is followed by external pelvic radiation.

Note. The ovaries must be removed because (1) they may contain microscopic metastases, and (2) the ovaries produce oestrogen which can stimulate any residual lesion.

Stage II

Total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH and B.S.O.) followed by external pelvic radiation or vaginal vault radiation. This line of treatment gives the same results of radical hysterectomy and pelvic lymphadenectomy (Wertheim operation) but it is preferred as the patient is elderly and may be diabetic, obese, and hypertensive i.e. poor operative risk.

Stage III

Treated by radiotherapy. The uterine cavity and vaginal vault are packed with radium or caesium followed by external pelvic radiation. However, this may be followed by TAH and B.S.O. if the tumour can be resected.

Stage IV

The lines of treatment include:

1. Hormonal therapy.
2. Chemotherapy.

3. Radiotherapy.
4. Pelvic exenteration.

Hormonal Therapy

Many adenocarcinomas of the endometrium (80%) have both oestrogen and progesterone receptors and are oestrogen dependent. Stage IV and recurrent cases are treated with large doses of progestogens. Medroxyprogesterone acetate can be given intramuscularly (Depo-Provera) or in the form of oral tablets (Provera tablets). The usual dose of Depo-Provera is 400 mg IM every week for 3 months then every 2 weeks. The tablets are given in a dose of 100 mg two or three times daily. Treatment is continued indefinitely if the tumour is responding. Progesterone antagonises oestrogen, inhibits DNA synthesis, and leads to atrophy of endometrial glands. If progestogen therapy fails or if the tumour cells have few or no progesterone receptors we give the antioestrogen tamoxifen (Nolvadex) or cytotoxic agents as a combination of cyclophosphamide, adriamycin and cisplatin (CAP-P stands for platinum) or a gonadotrophin releasing hormone analogue (agonist). The latter is injected monthly or every 3 months. It is supposed to have a direct effect on tumour cells. The dose of Nolvadex is 20-40 mg daily orally.

Palliative Radiotherapy

External radiation is given for recurrent pelvic masses and distant metastases.

Pelvic Exenteration

It is done in selected cases (see cervical carcinoma).

PROGNOSIS

When compared stage for stage, cervical and endometrial carcinoma have the same prognosis. However, the overall prognosis of endometrial carcinoma is better than cervical carcinoma as the majority of cases (75%) are in stage I when diagnosis is made. The reasons for good prognosis are; (1) the tumour is usually well differentiated; (2) it grows slowly; (3) spread by lymphatics occurs late in the disease; (4) early diagnosis and treatment as postmenopausal bleeding forces the patient to seek medical advice; (5) the tumour is hidden in the uterine cavity away from infection in the vagina.

The 5-year survival rate is as follows:

- Stage I: 80-90%
- Stage II: 60-70%
- Stage III: 30-40%
- Stage IV: 0-20%

Notes

- Metastasis may appear in the vaginal vault after hysterectomy for endometrial carcinoma. It is due to implantation of malignant cells during operation, or forcing the cells through lymphatics and veins by handling of the uterus or carcinoma cells were already present in the lymphatics at the

time of surgery (most common explanation). Postoperative radiation reduces the incidence of vault metastases from 10% to 1-2%.

- Factors which reduce the risk of E.C. are (1) the combined oral contraceptives; (2) smoking possibly through anti-oestrogenic effect.

UTERINE SARCOMAS

PATHOLOGY

Incidence. Uterine sarcoma is a rare tumour which occurs in about 2 per 100,000 women per year. It accounts for 1-3% of uterine cancers.

Age. The mean age is 55 years. However, it occurs at any age.

Aetiology. The cause is unknown. The predisposing factors are the same as in endometrial carcinoma and include excessive oestrogen, infertility, diabetes mellitus and obesity. Also previous radiation of the pelvis is present in about 20% of the cases.

CLASSIFICATION

The tumour may arise in the body of uterus or cervix. However the body is more frequently involved.

1. Pure homologous sarcomas. The tumour is composed of tissue which is of uterine origin:
 - a. Leiomyosarcoma.
 - b. Fibrosarcoma.
 - c. Endometrial stromal sarcoma which arises from endometrial stroma.
 - d. Angiosarcoma.
2. Pure heterologous sarcomas. The tumour is composed of tissue which is foreign to the uterus:
 - a. Chondrosarcoma.
 - b. Osteosarcoma.
 - c. Liposarcoma.
 - d. Rhabdomyosarcoma including sarcoma botryoides.
3. Mixed sarcomas:
 - a. Mixed homologous sarcomas.
 - b. Mixed heterologous sarcomas.
 - c. Mixed heterologous sarcomas with homologous elements.
4. Mixed mesodermal tumours. The tumour is a carcinosarcoma. It is composed of malignant epithelium (carcinoma) and malignant stroma (sarcoma). The epithelium arises from remnants of müllerian ducts and so the tumour is also called mixed müllerian tumour. There are 2 types:
 - a. Homologous type. It is carcinoma mixed with homologous sarcoma, e.g. leiomyosarcoma.



- b. Heterologous type. It is carcinoma mixed with heterologous sarcoma, e.g. chondrosarcoma.
5. Malignant lymphoma.

Note. Endometrial stromal sarcoma ESS is high grade or low grade. The latter has less than 10 mitoses per 10 HPF. The old name of ESS is endolymphatic stromal myosis. Leiomyosarcoma is the commonest malignant tumour of the uterus.

MODE OF SPREAD

1. Direct spread with invasion of tubes, ovaries, bladder, rectum, and intestine.
2. Bloodstream. All sarcomas spread mainly along blood vessels to distant organs as the liver, lungs, brain and bones.
3. Lymphatic spread to pelvic and aortic nodes.
4. Surface implantation (seeding). Malignant cells may be implanted into the peritoneal cavity leading to ascites and omental masses.

DIAGNOSIS

A. Symptoms

The patient may complain of one or more of the following:

1. Vaginal bleeding. It is the main symptom. It takes the form of menorrhagia, metrorrhagia, or postmenopausal bleeding. Prolonged blood loss leads to anaemia.
2. Vaginal discharge. With ulceration and infection it becomes blood stained and offensive and may contain necrotic debris. Occasionally, the patient passes a piece of polypoid growth per vagina.
3. Pelvic and abdominal pain.
4. Cachexia. It is due to repeated blood loss, infection, toxic absorption, pain and loss of sleep.

B. Signs

The uterus may be enlarged, and may form a pelvi-abdominal mass. Sarcoma botryoides arises from the cervix and by speculum examination it appears as a mass of soft pinkish polypi which resembles a bunch of grapes.

C. Investigations

1. Transvaginal sonography.
2. Endometrial biopsy is taken by one of 3 methods, fractional uterine curettage, endometrial aspiration, or by hysteroscopy.
3. Chest x-ray to exclude lung metastases.
4. Computed tomography (CT) scan to the pelvis and abdomen.
5. Magnetic resonance imaging which is more accurate than CT scan but it is costly.

STAGING

There is no staging system for uterine sarcomas. However, the FIGO staging for endometrial carcinoma is applied to uterine sarcomas.

TREATMENT

The treatment is total abdominal hysterectomy and bilateral salpingo-oophorectomy. This is followed by radiotherapy to the pelvis. Chemotherapy is given for advanced and recurrent cases. Combination therapy is better than single agents, e.g. a combination of vincristine, actinomycin D and cyclophosphamide (VAC) is given. Low grade endometrial stromal sarcoma is treated by TAH + B.S.O. followed by radiotherapy or progestogen therapy as the tumour is positive for oestrogen and progesterone receptors.

PROGNOSIS

It is very poor, no patient survives for 5 years. The 2 year survival rate is 45%. However, the prognosis is better with leiomyosarcoma occurring with a fibroid, mixed mesodermal tumours and low grade ESS.

GESTATIONAL TROPHOBLASTIC TUMOURS (DISEASE)

These arise from the placental trophoblast and are classified as:

1. Hydatidiform (vesicular) mole.
2. Invasive mole (chorioadenoma destruens).
3. Choriocarcinoma.
4. Placental site trophoblastic tumour.

CHORIOCARCINOMA

PATHOLOGY

Incidence

One case for every 5000 pregnancies in the Far East and one for every 50,000 pregnancies in Britain.

Origin

Choriocarcinoma is a malignant tumour of the trophoblast. About 50% of cases follow hydatidiform mole, 25% follow abortion, 23% follow normal pregnancy and 2% follow ectopic pregnancy. In rare cases, the tumour arises as a teratoma in the ovary or testicle.

Macroscopic Appearance

The tumour starts in the endometrium. It forms a soft friable dark red haemorrhagic mass projecting into the cavity of the uterus, sometimes forming a polyp. In some cases the tumour arises deep in the myometrium (intramural) and so it will not give rise to uterine bleeding

except late in the disease and curettage of the uterus will not show the tumour. The tumour secretes human chorionic gonadotrophin (HCG) which causes cystic changes in the ovaries in about 20% of cases. The cysts are lined by theca lutein cells. The tumour also secretes human placental lactogen and chorionic thyrotrophin.

Microscopic Appearance

The tumour consists of masses of cytotrophoblast (Langhans cells) and syncytium showing malignant characteristics. The blood vessels are eroded by the tumour and this causes the haemorrhagic naked-eye appearance. No chorionic villi are seen and this differentiates choriocarcinoma from invasive mole.

MODE OF SPREAD

1. Direct spread to reach other pelvic organs as the tubes, ovaries, and parametrium.
2. Bloodstream. The tumour disseminates early by the bloodstream to reach distant organs as the liver, lungs, brain, and bones. Retrograde venous spread may give rise to secondaries in the vulva and vagina.

SECONDARIES OF CHORIOCARCINOMA

These appear as dark red haemorrhagic nodules. They produce large amounts of human chorionic gonadotrophin. In rare cases the secondaries disappear after removal of the primary tumour. It is supposed that the body forms antibodies against chorionic tissue and these antibodies will overcome the secondaries after removal of the primary growth.

FIGO CLINICAL STAGING

Stage I: Tumour limited to the uterus.

Stage II: Tumour extends to the tube, ovary, broad ligament, or vagina by direct extension or by metastasis.

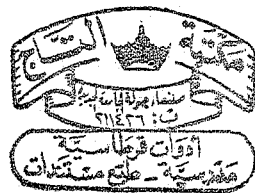
Stage III: Metastases to the lung.

Stage IV: Distant metastases with or without lung involvement.

DIAGNOSIS

A. Symptoms

1. Persistent or irregular uterine bleeding occurring after abortion, labour, or the evacuation of a vesicular mole. Bleeding occurs immediately or after several weeks or months, but rarely after 2 years. Vaginal bleeding is the commonest symptom.
2. Offensive blood stained vaginal discharge due to ulceration and infection of the tumour.
3. Amenorrhoea due to continuous production of HCG.
4. Acute abdominal pain due to perforation of the uterus by the growth and intraperitoneal haemorrhage, or due to rupture of the liver, rupture or torsion of a theca lutein cyst.
5. Patient may complain of abdominal or vaginal swelling.



6. Symptoms of secondaries may be the first manifestation of the disease as dyspnoea, haemoptysis (lung metastases), jaundice (liver metastases), and neurological symptoms as headache (brain metastases).

B. Signs

1. Cachexia and severe anaemia which is out of proportion to the amount of blood loss due to toxic absorption from the necrotic tumour and secondary infection.
2. Fever is common due to necrosis and infection.
3. The uterus may be of normal size or enlarged and soft.
4. The ovaries may be enlarged and cystic.
5. Haemorrhagic secondaries may be found in the vulva or vagina.
6. Hyperthyroidism is present in about 10% of cases.

C. Investigations

1. Uterine curettage. This should be done in every case of severe or persistent uterine bleeding occurring after abortion, labour or evacuation of hydatidiform mole. However, an intramural tumour will not be detected by curettage.
2. Estimation of HCG in serum or urine. It is essential for diagnosis, to determine the prognosis, and to follow the response to treatment. Radioimmunoassay is used to measure the beta subunit of HCG in serum.
3. Biopsy from metastases in the vulva or vagina.
4. Blood studies:
 - a. Complete blood count, and platelet count.
 - b. Electrolytes, liver function and renal function tests.
 - c. Thyroid function tests to diagnose the rare patient with secondary hyperthyroidism.
 - d. Blood grouping. Prognosis is bad if mother is group B or AB. Explanation is unknown.
5. Ultrasonography of the pelvis and abdomen to detect the tumour and to diagnose cysts in the ovaries. Doppler ultrasound to diagnose intramural tumour. Sonography also detects liver metastases.
6. Chest x-ray. About 80% of patients with choriocarcinoma have pulmonary metastases, and most of these are detected by routine chest x-ray which will reveal "cannonballs" or "snowstorm" appearance. When chest x-ray is negative, computed tomography (CT) or magnetic resonance imaging (MRI) is performed.
7. CT scan or MRI to detect metastases in the liver and brain.
8. Lumbar puncture with simultaneous estimation of HCG in serum and cerebrospinal fluid. It should be done if the brain scan is negative. In absence of brain metastases the concentration of HCG in the spinal fluid is low and the serum/CSF ratio is greater than 60:1, with metastasis the ratio is less than 60:1.
9. Electrocardiogram.

Notes

- The common sites of metastases are the lungs (80%), vagina (30%), brain (10%), and liver (10%).
- The patient may develop hyperthyroidism. HCG (like TSH) stimulates the thyroid gland. Also the trophoblast secretes chorionic thyrotrophin.

PROGNOSIS

A. **The high risk group.** Any of the following factors is associated with poor prognosis:

1. High level of HCG. Serum level greater than 40,000 mIU/ml. or urinary level more than 100,000 IU/L.
2. Symptoms of malignancy present for more than 4 months. This indicates delay in starting therapy.
3. The presence of metastases to sites other than lungs or vagina, i.e. brain, liver, or bowel metastases.
4. Failure of previous chemotherapy.
5. If the disease follows a full-term delivery. This indicates delay in diagnosis, as it is not easy to diagnose the condition during pregnancy also immunity is suppressed by pregnancy.

B. **The low risk group.** Patients in whom the above high risk factors are absent. This indicates good prognosis.

Note. mIU = milli international unit. mIU/ml is the unit of measurement in serum, and IU/L is the unit of measurement in urine.

TREATMENT

Choriocarcinoma should be managed in specialized centres. Treatment is by chemotherapy. The possible indications for hysterectomy include the following:

- a. Drug resistance or toxicity.
- b. If further children are not desired hysterectomy may be done during the first course of chemotherapy. This shortens the period of treatment with chemotherapy.
- c. Complications as severe uterine bleeding, perforation of the uterus with intraperitoneal haemorrhage, rupture or torsion of a theca lutein cyst.

The operation should be done during a course of chemotherapy to minimize dissemination of tumour emboli. The ovaries are left behind to avoid menopausal symptoms (ovarian metastasis is very rare).

Also surgical excision may be indicated for localized metastases in the vagina, lung, or brain if these lesions persist after chemotherapy (resistant cases) and in massive haemorrhage from the bowel.

Liver and brain metastases may bleed as a result of necrosis during the course of chemotherapy. So brain metastases should receive radiation, 2000-3000 rads "cGy" in combination with chemotherapy. Liver metastases receive radiation, 2000 rads only if they are extensive or subcapsular.

1. Treatment of Low Risk Group

A single cytotoxic drug is given, methotrexate or actinomycin-D. We start with methotrexate. However, in the presence of renal or hepatic impairment we start with or shift to actinomycin-D which is less toxic. Methotrexate is given IM or IV for 5 successive days, or it is given in combination with folinic acid. The course is repeated after the patient recovers from toxic symptoms usually every 10 days (but not less than 7 and not more than 14 days). The treatment courses are continued until β -HCG level becomes negative (undetectable). Once this level is reached, one more course is given. The HCG titre is measured once or twice weekly to detect the tumour response to therapy. The 5-year survival rate in the low risk group is about 97%.

2. Treatment of High Risk Group

Multiple agents are used. The MAC' triple therapy of Li consists of methotrexate, actinomycin-D, and cyclophosphamide given IV daily for 5 days. The course is repeated after patient recovers from toxic symptoms usually every 10 days. When the β -HCG level becomes negative we continue treatment by giving 3 more courses. If the triple therapy fails we give the modified Bagshawe Protocol (MBP), also known as EMA/CO protocol, where 5 chemotherapeutic agents plus folinic acid are used. This MBP can be used as the primary treatment in the high risk group. The 5-year survival rate in the high risk group is about 80%.

Modified Bagshawe (EMA/CO) protocol. Drugs used include etoposide, methotrexate, actinomycin-D, cyclophosphamide, oncovin which is vincristine, and folinic acid.

Methotrexate

Mode of Action

It is folic acid antagonist. It prevents the conversion of folic acid into folinic acid by inhibiting the enzyme dihydrofolate reductase. Folinic acid is necessary for the synthesis of DNA and RNA of the nucleus.

Methods of Administration

1. It is given IM or IV. Oral route is not preferred because of poor absorption. The dose is 0.4 mg/kg/day (20-25 mg) for 5 successive days, or;
2. 1 mg/kg/day is given IV or IM every other day alternating with folinic acid (leucovorin-citrovorum factor) as 0.1 mg/kg/day IM, IV or orally. 4 doses of each drug are given: methotrexate on days 1, 3, 5, 7 and folinic acid on days 2, 4, 6, and 8. This reduces the toxicity of methotrexate as folinic acid is the antidote.

Side Effects

It depresses the bone marrow leading to anaemia, leucopenia, and thrombocytopenia. Nausea, vomiting, diarrhoea, stomatitis, and ulceration of mouth and gastrointestinal tract. It is hepatotoxic and nephrotoxic.

Follow-up

After successful treatment (the HCG level remains negative for 3 successive weeks) the β -HCG is tested every month for one year then every 3 months for 5 years then every year for life. Oral contraceptive pills are given for 1 year to prevent confusion from a rising HCG levels due to pregnancy. After one year pregnancy can be allowed.

Note. Recovery from toxic symptoms is indicated by white cell count greater than $3000/\text{mm}^3$, granulocytes (polymorphonuclear leucocytes) greater than $1500/\text{mm}^3$, platelets greater than $100,000/\text{mm}^3$, normal liver and renal functions, recovery from stomatitis and gastrointestinal toxicity.

Placental Site Trophoblastic Tumour

The tumour is very rare, and is the rarest form of GTT. It arises from placental site after any form of pregnancy. However, the majority (95%) follow a full-term delivery, and few cases follow abortion or hydatidiform mole. Patient presents with either amenorrhoea or abnormal vaginal bleeding and uterine enlargement. The tumour consists of intermediate trophoblastic cells invading the myometrium. Chorionic villi are rarely seen. The intermediate trophoblast is not differentiated into cyto- or syncytiotrophoblast. The cells secrete small amounts of HCG, so the HCG level is normal or low usually $<3000 \text{ mIU/ml}$. The human placental lactogen may be elevated as some of the cells secrete this hormone. The tumour is locally malignant and may perforate the uterus. Distant metastases are rare (15%). The treatment is hysterectomy. Chemotherapy is only given for metastatic disease, as the tumour is generally resistant to chemotherapy.

Note for the postgraduate

Non-steroidal anti-inflammatory drugs decrease renal elimination of methotrexate and also displace it from albumin binding sites, thus enhancing its toxicity. So in the days following methotrexate treatment, patients should not receive these drugs. Also high-dose penicillins, sulphonamides, and omeprazole increase the toxicity of methotrexate.

ENDOMETRIOSIS AND ADENOMYOSIS**DEFINITION**

Endometriosis means the presence of endometrial tissue (glands and stroma) in abnormal sites, that is outside the normal uterine cavity. This ectopic endometrium responds to the ovarian hormones as the normal endometrium.

PREVALENCE

It is difficult to know the true prevalence because the disease is asymptomatic in many patients. However, the prevalence is about 5-10% in adult women and 20-40% in the infertile women.

SITES

A. Pelvic Endometriosis

(1) Peritoneal coat of the uterus; (2) cervix; (3) tubes; (4) ovaries; (5) pelvic peritoneum including Douglas and uterovesical pouches; (6) the uterosacral and round ligaments; (7) rectovaginal septum; (8) urinary bladder and ureters; (9) rectum and sigmoid colon; (10) vagina; (11) vulva.

B. Extrapelvic Endometriosis

(1) Umbilicus; (2) abdominal scar as after caesarean section; (3) abdominal viscera as gallbladder or appendix. Actually endometriosis can occur anywhere in the body even in the limbs.

The presence of endometrial tissue within the myometrium is called adenomyosis which is a separate entity from endometriosis and has a different aetiology. Adenomyosis and endometriosis never occur together, and the presence of one of them excludes the presence of the other. The commonest site of endometriosis is the ovary (40-75%), and the next common site is the peritoneum of Douglas pouch.

THEORIES OF AETIOLOGY

Endometriosis is explained by more than one theory because not all cases arise in the same way. However, the true cause is unknown.

1. **Tubal regurgitation theory of Sampson.** Retrograde menstruation may occur along the tubes so that fragments of endometrial tissue reach the peritoneal cavity and become implanted on pelvic organs. The menstrual blood falls first on the ovary and next into the pouch of Douglas to explain the most common sites of endometriosis. This theory cannot explain extrapelvic endometriosis or adenomyosis.
2. **Diverticular theory of Cullen.** The endometrial glands grow deeply into the myometrium in the form of diverticulae. The deep portions of the glands become separated from the surface endometrium forming areas of endometriosis between the muscle fibres. This explains adenomyosis.
3. **Serosal metaplasia theory of Meyer.** The peritoneum and uterine mucosa have the same embryonic origin (coelomic epithelium), so the peritoneum can undergo metaplasia into endometrial tissue. The same applies to the germinal epithelium of the ovary. The stimulus for this metaplasia may be hormonal or infection. It cannot explain lesions outside the abdomen and pelvis.
4. **The induction or combined theory of Lavender.** The regurgitated menstrual fragments stimulate the coelomic epithelium to undergo metaplasia.
5. **Halban theory.** Fragments of endometrium may spread by lymphatics or veins to reach any part of the body including the umbilicus which is connected with the pelvic lymphatics.

6. **Implantation theory.** Implantation of endometrial tissue may occur in abdominal scars after operations on the uterus as myomectomy or caesarean section. Also endometrial implantation may occur in a vaginal or perineal scar following childbirth and uterine curettage.
7. **Immunological theory.** There is failure of the cells of the immune system to eradicate endometrial implants.
8. **Genetic factor.** There is a familial tendency to develop endometriosis.

PREDISPOSING FACTORS

1. Hyperoestrinism. Excessive oestrogen is supposed to stimulate the growth of the abnormally placed endometrium. Endometriosis is frequently associated with other lesions caused by excessive oestrogen as fibroids and endometrial hyperplasia. Also the lesion undergoes atrophy after cessation of ovarian function.
2. Delayed marriage and infertility. These lead to prolonged action of oestrogen unopposed by progesterone which predominates during pregnancy.
3. Cervical obstruction due to stenosis, retroflexion of the uterus, and vaginal atresia predispose to retrograde menstruation.
4. Hysterosalpingography and curettage.

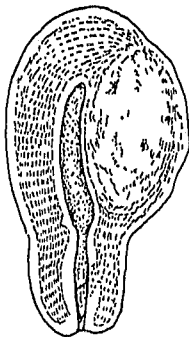
Note. Smoking reduces the incidence of endometriosis, fibroids, and endometrial carcinoma as it produces a hypoestrogenic state through inhibition of the ovary. Also smoking increases adrenal androgen production.

PATHOLOGY OF THE COMMON LESIONS OF ENDOMETRIOSIS

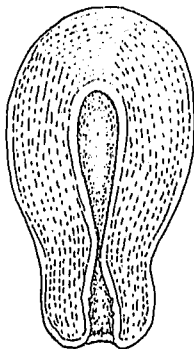
1. **Endometriosis of the ovaries.** The affected ovary is enlarged, irregular, and surrounded by adhesions. However, adhesions are absent in the early stage of the disease. The tunica albuginea is thickened and the ovary contains one or more cysts filled with dark brown blood and lined by endometrium. These are called "chocolate cysts" because of the colour of their contents. An ovarian endometrioma may reach 20 cm in diameter. Sometimes the lesion takes the form of small dark brown spots on the surface of the ovary. The condition is bilateral in about 50% of cases.
2. **Endometriosis of the pelvic peritoneum.** The lesion appears as dark-brown, black, or bluish nodules or small cysts containing old blood, and surrounded by a variable degree of adhesions. The lesions look like tobacco stains or powder burns (gun shot). Endometriosis can also appear as subtle (atypical – hard to identify) lesions including red implants, clear vesicles, or white plaques (scarred areas). The lesions may be seen on the peritoneum of Douglas pouch, uterovesical pouch, and the peritoneum covering the uterus and fallopian tubes. Sometimes, the lesions are accompanied by marked adhesions leading to fixed retroversion of the uterus.

Notes for the postgraduate

1. Microscopic endometriosis is defined as the presence of endometrial glands and stroma in a macroscopically normal pelvic peritoneum. It is found in about 15% of normal patients with normal laparoscopic findings.
2. Less than 1% of cases of endometriosis show malignant change into adenocarcinoma or endometrial stromal sarcoma.
3. Operations which may be complicated by endometriosis include caesarean section, abdominal myomectomy, abdominal subtotal hysterectomy, and uterine curettage which may lead to implantation of endometrial tissue in a vaginal or perineal scar. Also hysterosalpingography performed in the premenstrual week. When the uterine cavity is opened as in C.S. endometrial tissue may implant outside the uterus.



Localized



Diffuse

Fig. 97. Adenomyosis

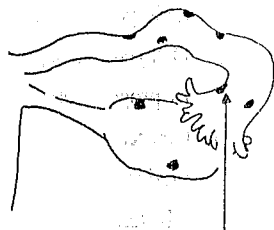


Fig.98. Foci of endometriosis

CLINICAL PICTURE

- Age. Most cases are seen in patients between 30 and 40 years. However, endometriosis has been reported in adolescents and in postmenopausal women receiving hormone replacement therapy.
- Parity. More common in nulliparae or women with low parity.
- Social and economic state. More common among the higher classes. It is described as “a disease of the rich”. This may be related to late marriage and late childbearing.
- Genetic factor. There is a familial tendency to develop endometriosis. Certain genes on chromosome 17 are related to the pathogenesis of endometriosis.
- Race. More in Japanese women.

Symptoms

The condition may be symptomless (15%). However, the patient may complain of one or more of the following depending upon the site of the lesion:

1. Dysmenorrhoea. Pain starts few days before menstruation due to congestion of ectopic endometrial glands and it increases in severity reaching its maximum at the end of menstruation due to distension of the glands with blood and then pain gradually diminishes after the period due to absorption of some of the blood within the glands. Dysmenorrhoea is progressive (crescendo dysmenorrhoea).

2. Chronic pelvic pain and backache, due to pelvic congestion, infiltration of uterosacral ligaments and increased production of prostaglandins.
3. Dyspareunia, due to endometriosis of the rectovaginal septum or Douglas pouch, prolapse of ovaries in Douglas pouch or retroversion of the uterus. Pain is severe before menstruation due to congestion of the glands.
4. Infertility. It is present in 30-40% of cases. The ectopic endometrium contains a high concentration of prostaglandin F2 alpha. Prostaglandins affect the ovum "pick up" and tubal motility and cause luteolysis (degeneration of the corpus luteum). The causes of infertility in endometriosis are:
 - a. Ovarian. Anovulation (it is rare and may be due to hyperprolactinaemia present in some cases), luteinized unruptured follicle (LUF Syndrome), or early degeneration of the corpus luteum causing luteal phase defect. The oocyte may be abnormal and not fertilized.
 - b. Tubal. Peritubal adhesions interfere with the "pick up" mechanism of the ovum also the prostaglandins affect tubal motility and ovum "pick up".
 - c. Uterine, due to retroversion.
 - d. Vaginal, due to dyspareunia.
 - e. Autoimmune mechanism. There is increase in the number of macrophages in the peritoneal fluid which phagocytose the sperms. In addition macrophages cause release of cytokines which may be toxic to the gametes. Also autoantibodies are present in about 60% of cases of endometriosis. These include antiphospholipid antibodies as anticardiolipin antibodies as well as other antibodies. These antibodies caused by the presence of ectopic endometrium may prevent implantation of the fertilized ovum leading to infertility or may cause repeated abortion.
5. Rupture of a chocolate cyst in the ovary gives rise to acute abdominal pain.
6. Endometriosis of the bladder gives rise to painful micturition and sometimes cyclic haematuria.
7. Endometriosis of the rectum causes painful defaecation (dyschezia) or even rectal bleeding during menstruation.
8. If there is endometriosis of the umbilicus or laparotomy scar, the patient notices a dark blue nodule which becomes tender, increases in size and may discharge blood during menstruation.
9. General ill-health and malaise are frequent with pelvic endometriosis. Intermittent pyrexia may occur at the time of menstruation due to absorption of retained blood (present in at least 10% of cases).

In fact endometriosis is associated with a characteristic triad of symptoms including dysmenorrhoea, dyspareunia, and infertility.

Notes

- Dyschezia is associated with endometriosis of the rectum, sigmoid colon, uterosacral ligaments (stretched during passage of faeces) and Douglas pouch.

- Types of pain associated with endometriosis include dysmenorrhoea, dyspareunia, dyschezia, dysuria, ovulation pain, chronic pelvic pain, low backache, and acute abdominal pain due to rupture of a chocolate cyst in the ovary.

Signs

1. The vulva, vagina, and cervix should be inspected for any sign of endometriosis.
2. Ovarian endometriosis. It is bilateral in about 50% of cases. The ovaries are felt as cystic tender masses which are fixed behind the uterus in Douglas pouch.
3. Endometriosis of the pelvic peritoneum. Multiple small firm tender nodules are felt through the posterior vaginal fornix. Similar nodules may be felt in the region of the uterosacral ligaments or rectovaginal septum or on the posterior surface of the uterus. These nodules are felt more easily on rectal examination.

In many women with endometriosis, no abnormality is detected during clinical examination.

INVESTIGATIONS

1. Laparoscopy. It helps to confirm the diagnosis and must be done before starting therapy. Small pelvic lesions are only diagnosed by laparoscopy carried out during the investigation of infertility or other complaint as unexplained chronic pelvic pain. A biopsy can be taken at the time of laparoscopy to confirm the diagnosis although it is not necessary.
The laparoscope is used to classify the disease into 4 stages – Stage I (minimal); stage II (mild); stage III (moderate); and stage IV (severe). This is the classification of the American Fertility Society and is done before starting therapy and to follow the response to treatment.
2. Ultrasonography. It diagnoses adenomyosis and detects the presence of ovarian chocolate cyst.
3. Magnetic resonance imaging. It can give accurate diagnosis.
4. Serum CA-125. It is elevated in moderate and severe cases, but normal in mild cases. It differentiates endometriosis from other pelvic lesions as benign ovarian cysts and used to monitor response to hormonal treatment.
5. Cystoscopy, proctoscopy or sigmoidoscopy may be needed to diagnose endometriosis of the bladder or bowel.
6. Histopathological examination of nodules excised from the umbilicus, abdominal scar, vagina or perineum.

DIFFERENTIAL DIAGNOSIS

1. Diffuse adenomyosis has to be differentiated from other causes of symmetrical enlargement of the uterus as submucous fibroid.

2. Ovarian endometriosis resembles ovarian cysts and chronic salpingo-oophoritis. In the latter, there may be a history of infection occurring after abortion, labour or gonococcal infection. The dysmenorrhoea is of the congestive type and the tubes are usually blocked. In endometriosis there is no history of infection, special type of dysmenorrhoea and the tubes are patent although they may be distorted by adhesions.
3. Endometriosis of the pelvic peritoneum. Multiple small firm tender nodules felt through the posterior vaginal fornix may be caused by endometriosis, tuberculous peritonitis, or secondaries from ovarian cancer.
4. Rupture of a chocolate cyst has to be differentiated from other causes of acute abdominal pain.
5. Carcinoma of the rectum and colon and diverticulitis.
6. All causes of intestinal obstruction.
7. All causes of haematuria. In endometriosis haematuria is limited to the time of menstruation.
8. All tumours of the umbilicus.
9. Swellings in the inguinal canal (endometriosis of the round ligament).

TREATMENT

1. No Treatment

Small symptomless lesions require no treatment, but the patient is kept under observation and examined every 6 months. Sometimes, the lesions become inactive after a time.

II. Nonhormonal Treatment

Indicated for small lesions with mild symptoms. Analgesics are given for pain. Prostaglandin inhibitors (naproxen, ibuprofen) are given for pain and menorrhagia. Because the condition improves as a result of pregnancy, young women are encouraged to conceive. During pregnancy the ectopic endometrium is changed into decidua followed by atrophy of the glands.

III. Hormonal Treatment

Indications: (a) Severe symptoms with small pelvic lesions, lesions more than 2 cm in diameter respond poorly to hormone therapy; (b) recurrence of symptoms after conservative surgery; (c) may be given for a short time (6-12 weeks) before surgery to make dissection easier; (d) after conservative surgery to allow any residual lesion to regress; (e) when operation is contraindicated or refused by the patient.

Hormonal treatment leads to improvement in 80% of cases and is followed by pregnancy in about 50% of the patients. The aim of hormone therapy is to induce pseudopregnancy or pseudomenopause. Mifepristone also leads to atrophy of the lesions.

1. Pseudopregnancy

Ovulation and menstruation are inhibited for 9 months (6-12 months) using a combined oral contraceptive or a progestogen alone to avoid the oestrogenic side effects. A combined contraceptive tablet is given daily. Oral medroxyprogesterone acetate (Provera tablets) is given in a dose of 10-30 mg daily, or dydrogesterone (Duphaston) tablets, 10-30 mg daily. To avoid daily intake of tablets, medroxyprogesterone acetate (Depo-Provera) is injected IM in a dose of 150 mg every 3 months, or a maximum dose of 150 mg every month to ensure amenorrhoea. The endometrium will undergo atrophy during the pseudopregnancy state. The side effects of progestogens include headache, weight gain, fluid retention, breakthrough bleeding, and depression which is a significant problem.

2. Pseudomenopause

- a. Danazol is given orally in a dose of 400-800 mg/day for 6-9 months. We usually start by 200 mg twice daily. The dose is increased if necessary to achieve amenorrhoea. Danazol is a weak synthetic androgen. It causes amenorrhoea and endometrial atrophy. The drug is expensive and has many side effects (see hormone therapy in Gynaecology).
- b. Gestrinone. It is a synthetic compound having the same action and side effects of danazol. The dose is 1.25-2.5 mg twice weekly for 6-9 months.
- c. A gonadotrophin releasing hormone analogue (agonist) can be given by daily nasal spray or intramuscularly or subcutaneously every 4 weeks for 6 months. The drug inhibits the secretion of pituitary gonadotrophins leading to amenorrhoea. Side effects include menopausal symptoms as hot flushes, dryness of the vagina, dyspareunia, and reduced libido. Treatment is limited to 6 months to avoid osteoporosis. The drugs are expensive. Nafarelin (Synarel) is given intranasally using a nasal spray, 200 micrograms twice daily. Goserelin (Zoladex), 3.6 mg injected subcutaneously every 4 weeks. Triptorelin (Decapeptyl) 3.75 mg injected intramuscularly every 4 weeks.
- d. Gossypole. It is extracted from cotton plant and used in China for treatment of endometriosis, fibroids, and menorrhagia. It inhibits the secretion of FSH and LH leading to amenorrhoea and endometrial atrophy. Dose is 20 mg orally daily for 2 months then 20 mg twice weekly for maintenance.

3. Mifepristone

It is given in a dose of 50 mg/day for 6 months. It causes significant atrophy of the lesion by direct inhibition of the endometrial cells.

IV. Surgical Treatment

It is indicated for large lesions and when hormonal therapy fails. Surgery is conservative or radical.

1. Conservative Surgery

In young patients below 40 years the aim of operation is to remove all areas of endometriosis leaving behind healthy ovarian tissue. Some advise removal of the appendix, even when it looks normal, as it is a likely site for endometriosis. Ventrosuspension by plication of round ligaments or uterosacral ligaments is done to correct retroversion after conservative surgery to improve fertility and prevent re-adherence of uterus and ovaries to Douglas Pouch. It also prevents tubal regurgitation and can arrest the progress of pelvic endometriosis. Presacral neurectomy may be done with conservative surgery to reduce severe dysmenorrhoea. In case of infertility, surgery is done using microsurgical technique to avoid postoperative adhesions.

With severe endometriosis, preoperative hormonal therapy (with danazol or gonadotrophin releasing hormone analogue) may be given to make surgery easier, or hormonal therapy is given postoperatively to allow any residual lesion to regress.

Patients become pregnant usually within 2 years in about 60% in mild cases, 50% in moderate cases, and 40% in severe cases.

Laser can be used at laparotomy or through the laparoscope to vaporize or excise areas of endometriosis. Also small implants in the pelvis can be destroyed with diathermy.

Tumours on the body surface e.g. in abdominal scar are excised.

2. Radical Surgery

When the patient is above 40 years the treatment is total abdominal hysterectomy and bilateral salpingo-oophorectomy. If the patient develops menopausal symptoms she receives oestrogen and progestogen with little risk of recurrence of endometriosis.

V. Radiological Treatment

Induction of artificial menopause by external pelvic radiation cures the condition by causing atrophy of endometrial tissue. It is applied only in patients above 40 in whom operation cannot be done as in case of wide spread pelvic endometriosis (frozen pelvis) or endometriosis of the rectovaginal septum which is difficult to excise surgically.

Notes for the postgraduate

1. All hormones used for treatment of endometriosis lead to suppression rather than cure of the disease. Recurrence of endometriosis occurs in a significant number of cases after cessation of any kind of hormonal treatment. The recurrence rate 5 years after hormonal treatment is 40% for mild disease and 75% for severe disease. Recurrence after surgery may be explained by incomplete excision, presence of microscopic endometriosis which escaped detection, or growth of a new lesion stimulated by any of the previously mentioned mechanisms.
2. Suppression of the disease and pregnancy rate are similar with all types of hormonal treatment. The drugs differ only in side effects and costs. Medroxyprogesterone acetate is often the first choice for hormonal treatment because of less side effects and cost compared with other hormones.

ADENOMYOSIS

It means the presence of endometrial glands and stroma within the myometrium. The exact aetiology is unknown but it can be explained by the Cullen diverticular theory.

PATHOLOGY

Adenomyosis may be diffuse or localized. In the diffuse type the uterus is slightly symmetrically enlarged and firm. It rarely exceeds the size of 12 weeks pregnancy. Occasionally, there is a localized area of endometriosis causing irregular enlargement of the uterus. On cut section the myometrium is thickened and shows a whorled appearance like that of a myoma but without a capsule. The presence of endometrial glands leads to proliferation (hyperplasia) of muscle and connective tissue fibres. Small dark brown spots are seen between the muscle fibres which are endometrial glands distended with blood. Sometimes the endometrial glands do not contain blood as the lesion arises from the basal endometrium which does not always respond to ovarian hormones due to lack of progesterone receptors. The cavity of the uterus is enlarged and the endometrium is thick and hyperplastic.

CLINICAL PICTURE

- Age. Most cases are seen in patients aged 40-50 years.
- Parity. Most of the cases (80%) are parous women.
- Social and economic state. More common among the lower classes.
- Associated lesions. Fibroids (in 50% of cases), and endometrial hyperplasia.

SYMPTOMS

Many patients (30-40%) are asymptomatic. However, the patient may complain of:

1. Menorrhagia. It is the main complaint. Adenomyosis leads to menorrhagia because of (a) increased vascularity of the uterus; (b) increased surface area of the endometrium; (c) the presence of endometrial hyperplasia; (d) impaired myometrial contractions caused by the presence of ectopic endometrium.
2. Dysmenorrhoea. It is a special type of dysmenorrhoea which is progressive (crescendo dysmenorrhoea). However, this special type of dysmenorrhoea may be absent in case of adenomyosis as the ectopic endometrium is composed of basal endometrium which does not always bleed as it is less responsive to ovarian hormones. In fact, not all endometriomas menstruate.

SIGNS

The uterus may be slightly symmetrically enlarged, firm and tender. It rarely exceeds the size of 12 weeks pregnancy. Occasionally, the uterus is asymmetrically enlarged due to a localized area of endometriosis or due to an associated fibroid. It may be fixed in retroversion if there is associated pelvic endometriosis.

INVESTIGATIONS

- Ultrasonography. It diagnoses diffuse adenomyosis. However, it is difficult to differentiate localized adenomyosis from a myoma. In this case, CT scan or MRI is helpful
- Magnetic resonance imaging. It can give accurate diagnosis.
- Histological examination of the uterus after hysterectomy is the only sure diagnostic method.

TREATMENT

1. Medical treatment. Analgesics for dysmenorrhoea. Antiprostaglandins improve both dysmenorrhoea and menorrhagia.
2. Severe menorrhagia is treated by dilatation and curettage.
3. Gonadotrophin releasing hormone analogues lead to amenorrhoea and decrease in uterine size. However, the effect is temporary and the uterus returns to its original size with the same symptoms after cessation of therapy.
4. Hysterectomy is the definite treatment.

Notes

- Progestogens are of no value in adenomyosis as the lesion is composed of basal endometrium which does not always respond to ovarian hormones due to lack of progesterone receptors.
- The main symptom of extrauterine endometriosis is dysmenorrhoea while it is menorrhagia in adenomyosis.
- Stromal adenomyosis. The endometrium spreading into the myometrium is composed mainly of endometrial stroma without endometrial glands. It may give rise to stromal sarcoma.

UTERINE POLYPI

Polypi may arise in the body or in the cervix.

(A) UTERINE BODY POLYPI

1. ADENOMATOUS OR MUCOUS POLYP

It arises from the endometrium. There are two types:

- a. Multiple polypi: These result from stimulation of the endometrium by excessive oestrogen as in case of metropathia haemorrhagica, fibroids and endometriosis. This is the commonest uterine body polyp.
- b. Single adenomatous polyp, which is an adenoma of the endometrium. It is composed of endometrial glands in a connective tissue stroma and covered by columnar epithelium.

Adenomatous polypi cause menorrhagia and sometimes intermenstrual bleeding. Diagnosis is easy if the polyp protrudes from the cervix, otherwise, diagnosis cannot be made except by uterine curettage, hystero-graphy or hysteroscopy.

Treatment is by uterine curettage. A single polyp is removed by sponge forceps or hysteroscope. Histopathological examination is necessary to exclude malignancy.

2. FIBROID POLYP

As a result of uterine contractions a submucous fibroid protrudes into the uterine cavity and develops a pedicle to form a polyp. The polyp may be forced through the cervix dilating it and may even appear at the vulva. The polyp forms a firm mass, its tip is liable to necrosis and infection due to poor blood supply. In very rare cases, the pedicle separates and the polyp is detached with spontaneous cure. This can only occur during the puerperium. A rare complication is chronic inversion of uterus.

Symptoms. (a) Menorrhagia; (b) irregular vaginal bleeding due to necrosis and ulceration of the tip of the tumour; (c) offensive vaginal discharge due to infection of the polyp; (d) colicky pain due to uterine contractions trying to expel the tumour.

Treatment. Vaginal myomectomy or hysterectomy.

3. PLACENTAL POLYP

If a placental fragment is retained in the uterus after an abortion or labour, blood becomes coagulated in layers over the retained fragment forming a polyp which is dark red in colour and firmly adherent to the wall of the uterus. The condition gives rise to irregular vaginal bleeding or menorrhagia after an abortion or labour. The uterus is subinvolved and the cervix may remain dilated. Treatment is curettage and histological examination to exclude choriocarcinoma.

4. MALIGNANT POLYPI

Malignant change may occur in a fibroid or adenomatous polyp. Primary malignant tumour as carcinoma, sarcoma or choriocarcinoma may form a polyp projecting into the uterine cavity.

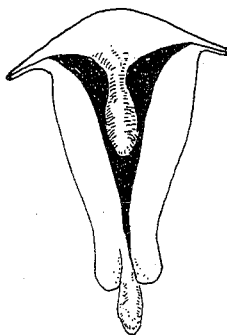


Fig.99. Uterine body and cervical polypi

(B) CERVICAL POLYPI

1. ADENOMATOUS OR MUCOUS POLYP

Pathology. It arises from the endocervix. In the majority of cases it is the result of chronic cervicitis as chronic infection stimulates proliferation of the endocervical epithelium. In some cases it is due to hyperoestrinism. The polyp is composed of cervical glands embedded in a connective tissue stroma and covered by columnar epithelium. The latter may undergo metaplasia into squamous epithelium as a result of infection. The polyp appears as single or multiple, soft swelling projecting from the external os.

Symptoms. Vaginal discharge and other symptoms of chronic cervicitis. A frequent symptom is contact bleeding.

Treatment. Surgical excision with cauterization of the base of the polyp to prevent recurrence. Curettage of the cervical canal is performed to prevent recurrence because there is usually hyperplasia of the endocervical mucosa. Uterine curettage is also done as the lesion may be associated with endometrial polypi. The removed polyp must be examined histologically to exclude malignancy.

2. FIBRO-ADENOMATOUS POLYP

It is an adenomatous polyp in which the stroma is dense and fibrous.

3. FIBROID POLYP

It is firm in consistency. It is attached by a pedicle to the cervical canal or it may arise from the ectocervix. The tip may undergo necrosis and infection and may resemble carcinoma of cervix.

4. MALIGNANT POLYPI

Carcinoma or sarcoma including the rare highly malignant sarcoma botryoides "grape-like sarcoma".

5. BILHARZIAL POLYPI

The patient is usually young with a history of bilharziasis as terminal haematuria. The polypi are single or multiple and firm in consistency. Biopsy confirms the diagnosis.

6. TUBERCULOUS POLYPI

Usually secondary to a tuberculous lesion elsewhere in the body. They are multiple, dark red in colour, and soft in consistency.



NEOPLASMS OF THE FALLOPIAN TUBE

I. BENIGN

Adenomatoid tumour is the commonest benign tumour of the tube. Other benign tumours include adenoma, papilloma, myoma, lipoma, haemangioma and lymphangioma.

The adenomatoid tumour of the tube is a small gray-white nodule, 1-2 cm in diameter. It is composed of small tubules lined by flat or low cuboidal epithelium. It is of mesothelial origin and does not turn malignant. The tumour can be present below the serosa of the fundus of the uterus.

II. MALIGNANT

1. Primary. Carcinoma (most frequently adenocarcinoma), sarcoma, and choriocarcinoma which may occur after tubal pregnancy. Sarcoma and choriocarcinoma are very rare.
2. Secondary. Secondary tumours are more common than the primary and account for about 85% of cases.

CARCINOMA OF THE FALLOPIAN TUBE

PATHOLOGY

Incidence. It is the rarest malignant tumour of the female genital tract and presents about 0.3% of all cases of genital tract cancers.

Age. The patient is usually postmenopausal. The commonest age incidence is 50-60 years.

Parity. About 50% of cases are infertile.

Macroscopic Appearance

The tumour is found in the middle or distal third of the tube. It is bilateral in 10-20% of cases. The tube is distended and appears sausage-shaped or retort-shaped like a hydrosalpinx. The tumour may protrude at the fimbrial end.

Microscopic Appearance

It is a papillary adenocarcinoma in the majority of cases (95%), rarely it is squamous cell carcinoma.

MODE OF SPREAD

1. Direct spread.
2. Lymphatic spread. It occurs early to the aortic lymph nodes and occasionally to the inguinal lymph nodes by lymphatics which accompany the round ligaments.

3. Bloodstream. Spread by bloodstream to distant organs as liver, and lungs occurs late when the disease is advanced. Retrograde venous spread leads to paraurethral (suburethral) vaginal metastases.
4. Surface implantation (seeding). It occurs via the tubal lumen into the peritoneal cavity.

FIGO STAGING

It is similar to that used for ovarian carcinoma.

DIAGNOSIS

A. Symptoms

1. Vaginal discharge. It is the main complaint. It is watery and escapes continuously or in gushes (hydrops tubae profluens). Later on, there is a blood stained discharge or frank bleeding from ulceration of the growth.
2. Dull aching or colicky pain in one or other iliac fossa. It is due to distension or contraction of the tube.

B. Signs

1. An adnexal mass is felt in more than 50% of the cases which is bilateral in 10-20% of patients. The disease is mostly mistaken for an ovarian tumour.
2. Ascites. It develops in advanced cases when the growth is exposed to the peritoneum.

Latzko syndrome consists of colicky pelvic pain, relieved by discharge of watery fluid from the vagina, and the presence of an adnexal mass. It occurs with tubal carcinoma and intermittent hydrosalpinx.

C. Investigations

1. Cervical smear. Malignant cells appear in about 20% of cases.
2. Laparoscopy. When done to diagnose an adnexal mass will show the tumour.

Note. The condition should be suspected when uterine curettage is negative in a woman suffering from postmenopausal bleeding.

DIFFERENTIAL DIAGNOSIS

1. Ovarian tumour.
2. Pelvic inflammatory disease including hydro- and pyosalpinx.

TREATMENT

The same treatment as ovarian cancer.

1. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and appendectomy are done if the case is operable. This is followed by chemotherapy.
2. Debulking (cytoreduction) operation. If it is impossible to remove the whole tumour, as much of the malignant tissue is removed including the uterus, tubes, ovaries, omentum,

appendix peritoneal and retroperitoneal implants, and bowel resection if the bowel is involved. This is followed by chemotherapy. Progestogens are useful as the tumour like endometrial carcinoma is oestrogen dependent.

3. Recurrent cases receive chemotherapy.

PROGNOSIS

It is based on the stage of the disease and is similar to ovarian cancer. However, because of late diagnosis the overall prognosis is bad and the 5-year survival rate for all stages is 20-30%.

OVARIAN NEOPLASMS

The ovary consists of 3 embryonic tissues; the coelomic epithelium, the germ cells (ova) and mesenchymal cells.

The coelomic epithelium forms the germinal epithelium and sex cords. The germinal epithelium covers the surface of the ovary. Sex cords give rise to granulosa cells in the female and Sertoli cells in the male.

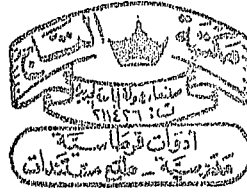
The mesenchymal cells form the fibroblasts of the ovarian stroma and theca cells in the female and Leydig cells in the male.

The germ cells are totipotent and can give rise to any tissue and the mesenchymal cells are multipotent which can give rise to many types of tissues. In fact any type of neoplasm can arise in the ovary. About 80% of ovarian neoplasms are cystic, and 20% are solid. The majority of solid neoplasms are malignant.

CLASSIFICATION

The following classification is accepted by the World Health Organization and the FIGO.

1. Epithelial tumours.
2. Sex cord and stromal tumours.
3. Germ cell tumours.
4. Lipid cell tumours.
5. Gonadoblastoma.
6. Soft tissue tumours not specific to the ovary.
7. Unclassified tumours.
8. Secondary (metastatic) tumours.



Notes

- Detailed classification is beyond the scope of the undergraduate student.
- Epithelial tumours include serous, mucinous, Brenner, endometrioid and clear cell (mesonephroid) tumours.
- Sex cord and stromal tumours arise from granulosa cells, theca cells, Sertoli cells, Leydig cells and fibroblasts (fibroma). They occur in pure or mixed types.
- Germ cell tumours include teratomas, choriocarcinoma, dysgerminoma, endodermal sinus tumour, embryonal carcinoma, polyembryoma and mixed forms.
- Tumour like conditions as follicular cyst, corpus luteum cyst, inclusion cyst, inflammatory cyst, polycystic ovaries, endometriosis and pregnancy luteoma.

PATHOLOGY AND CLINICAL FEATURES

Surface Papilloma

Small, often multiple and pedunculated with a connective tissue core.

Simple Serous Cyst (Cystoma Simplex)

Unilocular, very rarely multilocular, the wall is thin and lined by cuboidal or low columnar epithelium which may be ciliated. It contains clear serous (watery) fluid and never turns malignant. It is small in size and usually unilateral.

Papillary Serous Cystadenoma

Macroscopically, the tumour is multilocular, contains clear serous fluid and shows intracystic or extracystic papillae (endophytic or exophytic papillae). Microscopically, the cyst is lined by cuboidal or low columnar epithelium which may be ciliated resembling that of the fallopian tube. Psammoma bodies are characteristic of serous tumours. These are seen in the connective tissue stroma and appear as small spherical granules and are caused by deposition of calcium in degenerating epithelial cells. The clinical features are: (1) bilateral in 30-50% of cases; (2) ascites is common if there is external papillae; (3) rupture of the cyst may lead to implantation of the epithelium on the peritoneum with formation of papillae and persistent ascites; (4) malignant change is common and occurs in 30-50% of cases giving rise to papillary serous cystadenocarcinoma.

Mucinous Cystadenoma

Macroscopically, the tumour is multilocular, it contains mucin which coagulates in alcohol or formalin to form a jelly-like mass. Mucin is colourless but may be yellow, green or brown due to intracystic haemorrhage. Microscopically, the cyst is lined by tall columnar occasionally ciliated epithelium. Goblet cells are often present. The epithelium resembles that of the endocervix or intestine. The clinical features are: (1) it is the commonest ovarian neoplasm (accounts for about 20% of all ovarian tumours); (2) unilateral in the majority of cases (90%); (3) may reach a very large size filling the whole abdomen, the largest tumour recorded weighed 148 kg; (4) malignant change is rare (5-10%); (5) rupture of the cyst may lead to myxoma peritonei (jelly-belly) where the peritoneal cavity is filled with gelatinous mucin, because the epithelial cells become implanted on the peritoneum and continue to secrete and so the condition persists after removal of the primary tumour. The condition is treated by removal of the tumour and evacuation of the gelatinous material. This is followed by chemotherapy. Only 50% of patients survive for 5 years. Death is due to intestinal obstruction and wasting. Rupture of a mucocoele of the appendix or gallbladder may also lead to myxoma peritonei.

Note. There are many types of mucin: That found in mucinous tumours is a glycoprotein with a high content of neutral polysaccharides and is not precipitated by acetic acid. The old name was pseudomucin.

Brenner Tumour

A rare solid tumour, usually arises in women over 40. It is often less than 2 cm in diameter. In many cases, it is found in the wall of a mucinous cystadenoma. It consists of

groups of epithelial cells (transitional like that of the urinary tract or squamous) embedded in a connective tissue stroma and so macroscopically it resembles a fibroma. The epithelial cells have a "coffee bean" appearance due to longitudinal grooving of the nuclei. The tumour is unilateral, may secrete oestrogen and malignant change is very rare.

Endometrioid Carcinoma

It is an adenocarcinoma which resembles endometrial adenocarcinoma.

Clear Cell (Mesonephroid) Carcinoma

It is an adenocarcinoma characterized by the presence of clear or "hobnail" cells or both. The clear cells have clear or vacuolated cytoplasm. The cytoplasm is clear as it is rich in glycogen. The "hobnail" cells have scanty cytoplasm and a large protruding nucleus. The tumour can also arise in the vagina, cervix and endometrium. The vaginal and cervical forms were seen in young females who were exposed in utero to diethylstilboestrol.

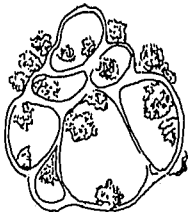


Fig.100 Papillary serous cystadenoma

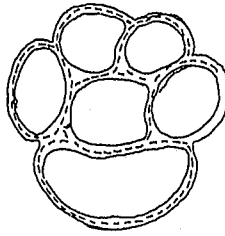


Fig.101. Mucinous cystadenoma

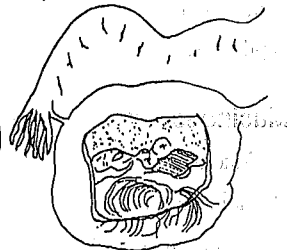


Fig.102. Dermoid cyst

Fibroma of the Ovary

It is a benign solid connective tissue tumour. It is firm in consistency. The surface is smooth and usually shows large dilated veins. The cut section shows a white whorled appearance. The tumour consists of bundles of spindle shaped fibroblasts in a dense connective tissue stroma. It is usually unilateral (90%) with a long pedicle. Ascites is present in about 20% of cases, and hydrothorax in 2% and is mostly on the right side but can be bilateral. The combination of ovarian fibroma, ascites and hydrothorax is known as Meigs syndrome. Ascites may be caused by mechanical irritation of the peritoneum by the heavy mobile tumour, loss of fluid from dilated veins on its surface or secretion by the tumour cells. Hydrothorax is due to transfer of fluid by lymphatics from the peritoneal cavity. Ascites and pleural effusion disappear after removal of the tumour. Less than 1% of fibromas are associated with Meigs syndrome. Malignant change is rare (0.5%). The combination of an ovarian tumour which is not fibroma with ascites and hydrothorax is called pseudo-Meigs syndrome. It can occur with granulosa cell, theca cell and Brenner tumours, and also with dysgerminoma and struma ovarii. The syndrome can also result from overstimulation of the

ovaries with gonadotrophins and with pedunculated subserous fibroid. The ovarian fibroma is liable to all types of degeneration that occur in the uterine myoma, except red degeneration.

Dermoid Cyst

It is a benign cystic teratoma. It is small or moderate in size, usually unilocular and is filled with thick yellow sebaceous material. A small mass of tissue is seen growing from the wall and is called the mammilla or embryonic node (Rokitansky tubercle) which is the centre of activity. The wall of the cyst is thick and is lined by stratified squamous epithelium (skin) or granulation tissue. The cyst may contain ectodermal structures as skin, hair and teeth, mesodermal structures as bone, cartilage and muscle, and endodermal structures as thyroid tissue and intestinal mucosa. There may be partial embryo formation (fetus in fetu). The clinical features are: (1) the tumour is slowly growing so it is small or moderate in size and seldom exceeds 12 cm in diameter; (2) bilateral in 10-15% of cases; (3) usually has a long pedicle and so it often lies in front or behind the uterus; (4) it occurs at young age (20-30 years) so it is the commonest ovarian tumour in young women and the commonest ovarian tumour met with during pregnancy; (5) malignant change is rare (1-3%) and will give rise to carcinoma, sarcoma or melanoma but usually squamous cell carcinoma; (6) rupture of the cyst leads to chemical peritonitis and dense adhesions because the sebaceous material is very irritant; (7) ultrasound or X-ray may reveal teeth.

Struma Ovarii

It is a benign teratoma which is composed mainly of thyroid tissue. It consists of acini containing colloid. It may produce thyroxine and cause thyrotoxicosis (5%) or turn malignant (5%). It may cause pseudo-Meigs syndrome.

Choriocarcinoma

It may start as a teratoma in which the trophoblastic tissue predominates or may follow an ovarian pregnancy. Also metastasis may occur from uterine choriocarcinoma. It secretes human chorionic gonadotrophin (HCG).

Feminizing Tumours

1. **The granulosa cell tumour.** It consists of cells similar to the granulosa cells of the graafian follicle. The cells are grouped around spaces suggestive of primordial follicles. The tumour produces oestrogens in large amounts. The tumour varies from a small nodule to a large swelling filling the whole abdomen. It is solid but may show cystic degeneration. The colour is white, yellow or orange depending on the amount of lipid content. It is malignant in about 25% of cases and is complicated by endometrial carcinoma in 15% of cases. If the tumour arises during childhood, it causes precocious puberty, during the childbearing period it causes irregular uterine bleeding, and after the menopause it causes postmenopausal bleeding.

2. **Theca cell tumour (Thecoma).** It consists of spindle shaped cells similar to theca interna cells and produces oestrogens. Solid in consistency. Colour is white, yellow or orange depending on the lipid content. Mostly seen after menopause. Malignant change is rare (5%). It may be difficult to differentiate it from fibroma.
3. **Mixed granulosa-theca cell tumour.** The tumour consists of both granulosa and theca cells.

Virilizing Tumours

1. **Sertoli cell tumour.** Benign, small and solid tumour, consists of tubules lined by Sertoli like cells. The tumour may be androgenic, oestrogenic or non functioning but usually oestrogenic (70%).
2. **Leydig cell tumour.** Also known as hilus cell tumour. It is a benign tumour and consists of Leydig like cells arranged in sheets or cords. The majority of these tumours are androgenic, few are oestrogenic or non functional.
3. **Sertoli-Leydig cell tumour.** Consists of Sertoli and Leydig like cells; known as androblastoma (formerly called arrhenoblastoma); commonly androgenic. About 5% of these tumours are malignant.
The virilizing tumours secrete androgens. This leads to defeminization, i.e. amenorrhea, atrophy of the breast and genital organs, followed by masculinization in the form of hirsutism, hoarseness of voice and enlargement of the clitoris.
4. **Gynandroblastoma.** A rare benign tumour that consists of granulosa or theca cells mixed with Sertoli or Leydig cells. The tumour may be oestrogenic or androgenic, but usually the latter.
5. **Adrenal-like tumour of the ovary.** It is composed of cells similar to those of adrenal cortex and arises from ovarian stromal cells.

Dysgerminoma

It occurs in the testicle or ovary, in the male, it is called seminoma of the testicle. It usually occurs in children and young women before the age of 30. It is a malignant solid ovarian tumour. The tumour consists of large round cells arranged in bundles or alveoli, embedded in a connective tissue stroma which is infiltrated with lymphocytes. It is bilateral in 10-15% of cases and occasionally occurs in association with testicular feminization syndrome or gonadal dysgenesis, especially with a Y chromosome. However, most dysgerminomas arise in normal ovaries. The tumour arises from the germ cell and may be mixed with other germ cell tumours e.g. dysgerminoma-choriocarcinoma. Dysgerminoma spreads mainly by lymphatics. It secretes placental alkaline phosphatase and lactic acid dehydrogenase enzymes.

Endodermal Sinus Tumour

It is composed of microcysts lined by flat cells. In many cases single papillae covered by flat epithelium with a central blood vessel project into the microcytes. These glomerulous like

structures are known as Schiller-Duval bodies. Most cases occur before the age of 20. It is the most malignant ovarian tumour. It is also called yolk sac tumour. It secretes alpha-fetoprotein. It is always unilateral.

Embryonal Carcinoma

It resembles embryonal carcinoma of the testis. It consists of large malignant cells which form solid areas or glands. The cells secrete alpha-fetoprotein. Areas of trophoblast are present in most cases, and secrete HCG.

Gonadoblastoma

It is a benign tumour composed of cells like those of dysgerminoma and granulosa or Sertoli cells. In most cases it occurs in abnormal, i.e. dysgenetic gonads and the patient mostly has a Y chromosome.

Polyembryoma

A highly malignant tumour which consists of embryonic structures like yolk sac, amniotic sac, embryonic disc, trophoblast and mesenchymal cells.

ORIGIN OF OVARIAN NEOPLASMS

Epithelial Tumours. These account for about 90% of all ovarian neoplasms and arise from the epithelium covering the surface of the ovary or from the epithelium forming the Walthard inclusion cysts. This surface epithelium has the same embryonic origin as the epithelium lining the müllerian ducts (both are coelomic in origin). Serous cysts are lined by epithelium similar to tubal epithelium and the epithelium lining mucinous cysts resembles endocervical mucosa while endometrioid carcinoma resembles endometrial adenocarcinoma.

Connective Tissue Tumours. These arise from ovarian stroma.

Germ Cell Tumours. These arise from the ovum (germ cell) by a process of parthenogenesis which means that the unfertilized ovum attempts to form an embryo (asexual reproduction).

Sex Cord and Stromal Tumours. The group of cells known as sex cords give rise to granulosa cells and Sertoli cells, while the gonadal mesenchymal cells (stromal cells) give rise to theca cells, Leydig cells and fibroblasts. These tumours are sometimes called mesenchymomas and they secrete sex hormones.

BENIGN OVARIAN NEOPLASMS

DIAGNOSIS

A. Symptoms

The condition may be symptomless and discovered accidentally, however, the patient may complain of one or more of the following:

1. Abdominal swelling which is the main complaint.
2. Pressure symptoms, a large abdominal tumour may cause dyspnoea, palpitation and dyspepsia. Tumour impacted in the pelvis causes rectal or bladder symptoms as retention of urine.
3. Pain, it is absent unless there is a complication as torsion, infection or malignancy.
4. Menstruation is not affected by benign or malignant tumours, even if bilateral, because there is always healthy ovarian tissue. However, menstruation is affected by functioning tumours.
5. Ovarian cachexia occurs with malignant tumours and sometimes with large benign ones because the large tumour interferes with digestion and absorption and because of the metabolic demands of the growing tumour.

B. Signs

1. Abdominal Tumours

There is a pelvi-abdominal swelling which is smooth or irregular if multilocular. It is cystic in consistency, in the majority of cases, however, solid areas may be felt in the cystic mass and sometimes the whole tumour is solid. The swelling is not tender unless there is a complication as infection or malignancy. It is dull on percussion. The flanks are resonant unless there is associated ascites. Vaginally, the lower pole may be palpated and it is felt separate from the uterus.

2. Pelvic Tumours

Bimanually, the tumour is felt to one side of the uterus. It does not move with movement of the cervix. If it has a long pedicle it may be felt in front or behind the uterus. It is mobile unless fixed by adhesions.

C. Investigations

1. Ultrasonography. It diagnoses that the swelling is ovarian in origin, cystic or solid, and benign or malignant. Suggestive features of malignancy include multiloculation, thick irregular septa, presence of solid areas, fungation of the tumour through the ovarian capsule, fixation and attachment to surrounding structures and the presence of ascites. It detects ascites before it is clinically apparent. With transvaginal Doppler ultrasound, the findings suggestive of malignancy include irregular distribution and formation of new blood vessels leading to increased blood flow and reduced resistance index to be 0.4 or

- less. Ultrasound may show liver metastases in case of malignancy. It also diagnoses hydronephrosis and hydronephrosis.
2. Plain X-ray to the abdomen may show teeth in a dermoid cyst. This has been replaced by ultrasound.
 3. Laparoscopy to diagnose a small ovarian tumour when ultrasound fails to differentiate it from a subserous fibroid or tubal inflammatory mass.

DIFFERENTIAL DIAGNOSIS

A. Large Ovarian Cyst

(1) Full bladder; (2) fetus (pregnancy); (3) fibroid if degenerated and cystic; (4) fluid; ascites and encysted tuberculous peritonitis; (5) fatty patient (obesity); (6) flatulence; (7) faecal mass (loaded sigmoid); (8) false pregnancy (pseudocyesis); (9) hydronephrosis in a mobile kidney; (10) pancreatic or mesenteric cyst; (11) hydatid cyst; (12) retroperitoneal tumour as fibroma or sarcoma.

B. Small Ovarian Tumour

(1) Full bladder; (2) fibroid; (3) tubal swelling as hydrosalpinx, pyosalpinx and ectopic pregnancy; (4) paraovarian cyst; (5) pelvic haematocoele and abscess; (6) incarcerated retroverted gravid uterus; (7) pelvic kidney; (8) tumour of rectum and pelvic colon; (9) diverticulitis; (10) retroperitoneal tumour.

Note. The patient must empty the bladder before gynaecological examination to avoid confusion with a full bladder.

TREATMENT OF BENIGN OVARIAN NEOPLASMS

Any solid ovarian tumour must be removed. Also any ovarian cyst larger than 5 cm in diameter, or if multilocular must be removed even if it is symptomless because we cannot be sure that it is not malignant or it will not turn malignant and to avoid complications as torsion. However, if there is a small ovarian cyst less than 5 cm in diameter, the patient is kept under observation. If it is a functional cyst it will decrease in size or disappear within 2 months. However, if the cyst persists or increases in size, it is considered a cystic neoplasm and must be removed. A combined oestrogen-progestogen contraceptive tablet helps regression of a functional cyst by inhibiting the secretion of pituitary gonadotrophins which may be the stimulus for cyst formation. A benign ovarian tumour is treated by:

1. Ovarian Cystectomy or Ovariectomy

The cyst or tumour is removed leaving behind healthy ovarian tissue. It is the operation of choice in a young woman, especially if the tumour is bilateral as in case of dermoid cyst.

2. Ovariectomy

It means removal of the whole ovary with the tumour. Indicated if the tumour has destroyed the whole ovary. The pedicle of the tumour is made of 3 parts; the ovarian ligament, the mesovarium and the infundibulo-pelvic ligament. The pedicle must be transfixed and ligated to avoid slipping of ligatures.

3. Total Abdominal Hysterectomy and Bilateral Salpingo-Oophorectomy

Indicated in a patient over 45 years even if the tumour is benign and unilateral for fear of malignancy.

Notes

- Oophorectomy means removal of an ovary which is not diseased.
- Tapping of the Ovarian Cyst. The aim of tapping is to remove a large ovarian cyst through a small abdominal incision. An ovarian trocar and cannula is used to puncture the cyst and evacuate its contents. The disadvantages are: (1) the cyst may be malignant and tapping can lead to dissemination of malignancy; (2) the cyst may be infected with liability to peritonitis; (3) it may be multilocular and difficult to empty; (4) the contents may be thick and cannot be evacuated. Tapping may be permissible in young women below 40 and also when the cyst looks benign.

MALIGNANT OVARIAN NEOPLASMS

INCIDENCE

The incidence of ovarian cancer ranges between 5-15 cases per 100,000 females per year. It comprises 20% of all genital tract cancers.

AGE

The commonest age incidence is 40-60 years. About 60% of cases occur between ages 40-60, 20% before age 40 and 20% after age 60.

PREDISPOSING FACTORS

The more frequently the patient ovulates, i.e. incessant ovulation, the greater the risk of developing cancer. Ovulation causes traumatic irritation of the covering ovarian epithelium. The predisposing factors include:

(1) Nulliparity; (2) infertility; (3) first pregnancy occurring after the age of 30; (4) early menarche and late menopause; (5) more than 40 years of ovulation; (6) ovulatory drugs as Clomid (not definitely proven); (7) excessive fat intake and obesity; (8) family history of ovarian cancer, or breast/ovarian cancer syndrome, or Lynch II syndrome; (9) exposure to asbestos; (10) regular dusting of the genital area with talc powder; (11) high social class; (12) previous pelvic radiotherapy, e.g. for cervical carcinoma; (13) polycystic ovarian syndrome.

PROTECTIVE FACTORS

1. Factors which reduce the rate of ovulation or inhibit it. These include (a) multiparity; (b) pregnancy before the age of 30; (c) early menopause; (d) use of combined contraceptive tablets.

2. A diet rich in vitamin A and fibre.
3. Mumps oophoritis. It protects through reduction of future ovulation. However, this is a matter of controversy as some believe that the mumps virus predisposes to ovarian cancer by causing ovarian damage.
4. Prophylactic oophorectomy. A unilateral benign ovarian tumour in a patient above 45 years is treated by total hysterectomy and bilateral salpingo-oophorectomy. Also if the uterus is removed for a benign lesion as fibroids or adenomyosis, both ovaries are removed if the patient is postmenopausal or has reached the age of 50 even she is still menstruating.

Notes

- Lynch II syndrome. It is hereditary non-polyposis colorectal cancer (HNPCC) which is associated with cancer in other sites of the body as the breast, ovary, endometrium, gastrointestinal tract as liver, kidney, or brain. It occurs in first and second degree relatives. Lynch I syndrome is isolated HNPCC which is not associated with any other cancer.
- Talc powder may migrate along the vagina, uterus, and fallopian tubes to reach the pelvic peritoneum and ovaries, and induce malignancy.

PATHOLOGY

I. Carcinoma of the Ovary

It may be primary or secondary.

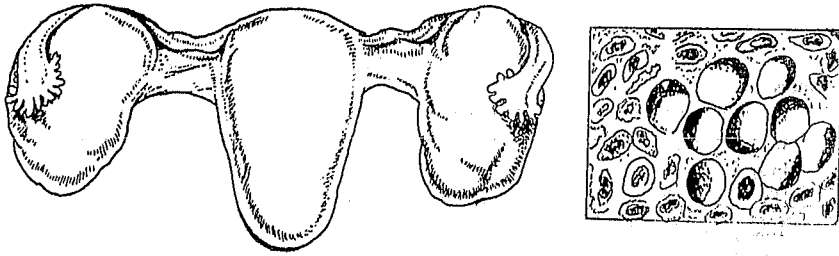
A. Primary Ovarian Carcinoma

It is bilateral in 80% of cases. This bilaterality is explained by the presence of multiple malignant foci at the same time and transfundal lymphatic spread from one ovary to the other. The tumour may be cystic or solid. Cystic carcinoma as papillary serous cystadenocarcinoma and mucinous cystadenocarcinoma. Solid carcinoma may take the form of endometrioid carcinoma, alveolar, scirrhus or clear cell carcinoma (mesonephroma) which is considered a variant of endometrioid carcinoma. Endometrioid carcinoma resembles endometrial adenocarcinoma. It arises as a primary tumour or as a malignant change in ovarian endometriosis which is rare.

B. Secondary Ovarian Carcinoma

It is nearly always bilateral. The ovary is a common site for metastases because it is rich in blood and lymphatic vessels. About 20% of all cases of ovarian cancer are secondary to a primary lesion elsewhere. The primary tumour is usually in the genital tract (tube, uterus and opposite ovary), the gastrointestinal tract (stomach, small intestine, colon or gallbladder), or the breast. However, any tumour can metastasize to the ovary. Secondaries may be typical or atypical. Typical secondaries are histologically similar to the primary tumour. Atypical secondaries are called Krukenberg tumour which is histologically different from the primary tumour. Krukenberg tumour is a solid, moderate in size, lobulated, kidney shaped tumour with a smooth surface, and freely mobile due to absence of adhesions. It is usually bilateral.

Microscopically, the tumour consists of groups of epithelial cells in a connective tissue stroma. The cells secrete mucus and the nucleus is displaced to one side of the cell (signet-ring cells). The primary tumour is a mucus secreting adenocarcinoma, usually in the stomach (75%) but sometimes in the colon, gallbladder, breast, or cervix. The primary tumour is often silent without symptoms. Metastasis occurs by retrograde lymphatic spread or by bloodstream and not by surface implantation due to deep location of malignant cells and absence of surface adhesions.



Signet-ring cells

Fig.103. Krukenberg tumours

II. Sarcoma of the Ovary

It is very rare. The commonest variety is spindle cell sarcoma. Teratoid sarcomas as rhabdomyosarcoma and fibrosarcoma may occur. Burkitt lymphosarcoma is common in children in certain parts of tropical Africa. It has a geographical distribution as malaria. It is caused by a virus (Epstein-Barr) carried by mosquitoes. The lesion starts in the jaw or in the ovaries. Leukemias and lymphomas also metastasize to the ovary.

MODE OF SPREAD OF OVARIAN CANCER

1. **Direct Spread;** to any neighbouring organ or tissues as tube, uterus, bladder, intestine, omentum and lateral pelvic wall.
2. **Lymphatic Spread.** (a) Along ovarian lymphatics which accompany the ovarian blood vessels to reach the para-aortic nodes then to mediastinal nodes and left supraclavicular gland (gland of Virchow); (b) to the inguinal lymph nodes along the round ligaments; (c) to the other ovary along the transfundal lymphatics; (d) spread to obturator, internal, external and common iliac lymph nodes on the same side of the tumour.
3. **Spread by the bloodstream;** to distant organs as liver, lungs and bones. This occurs late when the disease is advanced.
4. **Surface implantation or seeding;** to the tubes, uterus, peritoneum, omentum, liver and diaphragm. This transcoelomic spread is the commonest route of spread. Exfoliated malignant cells circulate with the peritoneal fluid to implant on the surface of organs in the pelvis and abdominal cavity.

DIAGNOSIS

I. Symptoms

The condition may be symptomless and discovered accidentally. In fact, many cases of ovarian cancer (75%) are found in an advanced stage (stage III or IV) when the diagnosis is made. For this reason, the disease is referred to as "The Silent Killer". The patient may complain of one or more of the following:

1. Abdominal swelling.
2. Pressure symptoms, a large abdominal tumour may cause dyspnoea, palpitation and dyspepsia. Tumour impacted in the pelvis causes rectal or bladder symptoms as retention of urine.
3. Dull aching pain or discomfort in the lower abdomen or pelvis. Severe pain occurs in case of complications as torsion, rupture or haemorrhage.
4. Menstrual function is not affected by malignant tumours even bilateral because there is always healthy ovarian tissue. However, menstruation is affected by functioning tumours.
5. Cachexia.
6. Irregular or postmenopausal uterine bleeding caused by secondaries in the uterus, coexistent uterine tumour or oestrogenic tumour.
7. Symptoms due to secondaries in the liver, lungs, and bones may be present.

II. Signs

The following clinical signs are suggestive of malignancy.

A. General Signs

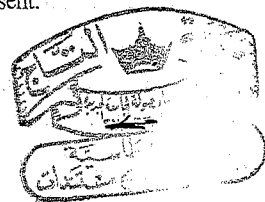
(1) Age. Extremes of age. If the age of the patient is above 50 years the chance of malignancy is over 50%, also tumours in childhood are usually malignant; (2) presence of cachexia; (3) oedema of the vulva, and legs especially if unilateral and varicosities; (4) enlargement of the gland of Wirchow (left supraclavicular lymph node). Enlarged Wirchow node is known as Troissier sign.

B. Abdominal Signs

(1) Rapid growth; (2) tenderness over the tumour; (3) fixation of the tumour; (4) bilateral tumours; (5) solid consistency or the presence of solid areas in a cystic tumour; (6) ascites; (7) secondary nodules (sister Mary Josef nodule) may be seen in the region of the umbilicus (cancer cells spread by lymphatics which accompany the obliterated umbilical arteries and the urachus); (8) enlargement of inguinal lymph nodes.

C. Local Signs

(1) Irregular uterine bleeding and postmenopausal bleeding; (2) the presence of firm nodules in Douglas pouch; (3) cervical smear may help if the tumour cells are exfoliated and reach the cervix. This reveals cancer cells in only 10-20% of cases.



Note. The presence of ascites usually indicates peritoneal metastases or the tumour has perforated the ovarian capsule.

III. Investigations

1. Ultrasonography (see benign neoplasms).
2. CT scan or MRI to the pelvis and abdomen to determine the extent of the disease. These are more accurate than ultrasonography.
3. Chest X-ray for lung metastases.
4. Intravenous pyelogram to show the course of the ureter which may be displaced by the tumour, to exclude hydronephrosis and to assess kidney function.
5. Barium meal or gastroscopy and barium enema or colonoscopy if a primary tumour is suspected in the stomach or colon.
6. Mammography if there is any breast mass to rule out primary breast carcinoma (presence of genetic links).
7. A cervical smear is taken.
8. Endometrial biopsy or uterine curettage if there is abnormal uterine bleeding to detect primary, secondary, or coexisting cancer.
9. Examination of pleural effusion for malignant cells. If present, the disease is stage IV.
10. Examination of serum for tumour markers. To monitor response to treatment and to detect recurrence.
 - a. CA-125 (cancer antigen-125), raised in nonmucinous epithelial carcinoma (>35 U/ml).
 - b. CA-19-9, raised in mucinous carcinoma.
 - c. CEA (carcinoembryonic antigen), raised in mucinous carcinoma.
 - d. Alpha-fetoprotein, human chorionic gonadotrophin, placental alkaline phosphatase, and lactic acid dehydrogenase for germ cell tumours.
11. Laboratory tests. (a) Complete blood count; (b) urinalysis; (c) fasting blood sugar; (d) renal function tests; (e) liver function tests; (f) serum electrolytes.
12. Electrocardiogram.

Notes

- Tapping of ascitic fluid (paracentesis) is not recommended as it does not preclude surgery, malignant cells are not detected in 40% of cases, the trocar may rupture the tumour, and implantation of malignant cells may occur along the insertion site.
- Bowel should be prepared before surgery.

DIFFERENTIAL DIAGNOSIS

1. Endometrial carcinoma metastasizing to the ovary.
2. Uterine fibroid may simulate a solid ovarian tumour and if it has undergone cystic degeneration may be mistaken for ovarian cyst.
3. Ovarian endometriosis.
4. Chronic pelvic inflammatory disease.
5. Tumours of the rectum and pelvic colon.

6. Extragenital tumours e.g. in the stomach may not be suspected till secondary tumours are discovered in the ovaries.
7. Other causes of ascites.

FIGO STAGING FOR PRIMARY OVARIAN CARCINOMA (1986)

The stages are based on findings at operation.

Stage I: Tumour limited to the ovaries.

IA: Tumour limited to one ovary; capsule intact, no tumour on ovarian surface; no malignant cells in ascites or peritoneal washings.

IB: Tumour limited to both ovaries; capsules intact, no tumour on ovarian surface; no malignant cells in ascites or peritoneal washings.

IC: Tumour limited to one or both ovaries with any of the following: capsule ruptured; tumour on ovarian surface; malignant cells in ascites or peritoneal washings.

Stage II: Tumour involves one or both ovaries with pelvic extension.

IIA: Extension and/or metastases to the uterus and/or tube(s); no malignant cells in ascites or peritoneal washings.

IIB: Extension to other pelvic tissues (e.g. pelvic nodes, pouch of Douglas), no malignant cells in ascites or peritoneal washings.

IIC: Pelvic extension (IIA or IIB) with malignant cells in ascites or peritoneal washings.

Stage III: Growth involving one or both ovaries with peritoneal implants outside the pelvis, or positive retroperitoneal or inguinal nodes, or extension to omentum or small bowel, or superficial liver metastasis.

Stage IV: Growth involving one or both ovaries with distant metastases including parenchymal liver metastasis or pleural effusion containing malignant cells.

SIGNS OF MALIGNANCY AT OPERATION

(1) The presence of ascites, especially if blood stained and the ascitic fluid is examined for malignant cells. In the absence of peritoneal fluid, saline washings of the pelvic cavity, paracolic gutters and right subdiaphragmatic area are similarly examined; (2) presence of adhesions; (3) bilaterality of the tumour; (4) solid consistency or the presence of solid areas in a cystic tumour; (5) extracystic papillae; (6) large blood vessels on the tumour surface; (7) areas of haemorrhage and necrosis in the tumour; (8) fungation of the tumour through its capsule; (9) the presence of peritoneal nodules, metastases in the liver, omentum or Douglas pouch; (10) enlargement of the para-aortic glands; (11) in case of doubt, a frozen section is examined.

TREATMENT OF OVARIAN MALIGNANCY

A. Prophylactic Treatment

1. Any solid ovarian tumour must be removed.
2. Any ovarian cyst larger than 5 cm in diameter, or if multilocular must be removed.
3. Any ovarian tumour after menopause must be removed irrespective of its size.
4. A unilateral benign ovarian tumour in a patient over 45 years is treated by total hysterectomy and bilateral salpingo-oophorectomy.
5. If the uterus is removed for a benign uterine lesion as fibroids or adenomyosis, the ovaries are removed if the patient is postmenopausal or has reached the age of 50 even if she is still menstruating.
6. Women with a family history of ovarian cancer are recommended to have prophylactic oophorectomy when they reach the age of 40. The laparoscope may be used for oophorectomy.
7. Prophylactic oophorectomy is also recommended for women with breast cancer gene 1 or gene 2 mutation (BRCA1 or 2 mutation) when they reach the age of 40.

B. Active Treatment

1. Surgery

It is the primary treatment. The abdomen is opened by a vertical midline incision to allow exploration of the upper abdomen. Peritoneal washings are done if there is no ascitic fluid available for cytological study. In this case, 100 ml of normal saline is instilled into the pouch of Douglas and into each of the paracolic gutters, and the right subdiaphragmatic area and then withdrawn for cytological examination. This is followed by full exploration of the pelvis and abdomen to stage the disease (examination of uterus, tubes, ovaries, bladder, pelvic peritoneum, pelvic lymph nodes, omentum, stomach, small and large bowel and its mesentery, liver, diaphragm and para-aortic lymph nodes). The treatment depends upon the stage of the disease.

A. Stage I

The treatment is total hysterectomy, bilateral salpingo-oophorectomy, omentectomy and appendectomy (the appendix may be the site of a primary tumour or metastasis). This is followed by chemotherapy. The omentum (greater omentum) must be removed in every case because it is a common site for minute metastases and by its removal we reduce the bulk of the tumour and this improves the result of postoperative chemotherapy. Surgery alone is done without adjuvant therapy if the tumour is stage IA Grade 1 (G1 = well differentiated tumour).

Conservative Surgery

Unilateral salpingo-oophorectomy without adjuvant therapy can be undertaken provided the following conditions are fulfilled.

- a. Young patient who wants to keep her fertility.
- b. The tumour is stage IA Grade 1 or borderline.

- c. The other ovary looks normal by the naked eye (wedge biopsy or bisection of the ovary is not done to exclude malignancy as this leads to adhesions and infertility).

Frozen sections are done to know the diagnosis during surgery. Also young patient with a germ cell tumour (as dysgerminoma) or granulosa cell tumour or Sertoli-Leydig cell tumour can be treated in the same way provided the above criteria are fulfilled.

Once childbearing is completed, hysterectomy with removal of the other ovary is recommended.

B. Stage II, III and IV

The treatment is debulking operation (cystoreduction) to remove as much of the malignant tissue including the uterus, tubes and ovaries with omentectomy, appendectomy, removal of peritoneal and retroperitoneal implants and bowel resection if the bowel is involved. This cytoreduction is followed by chemotherapy. The aim of cytoreduction is to leave residual lesions less than 1 cm in diameter to improve the prognosis.

2. Chemotherapy

Treatment with a combination of cisplatin (or carboplatin) and paclitaxel gives better results compared with other drugs. The 2 drugs are given intravenously for one day, and repeated every three weeks for 6 cycles. Paclitaxel is highly toxic and expensive. If the patient is old or weak, a single agent as cisplatin or carboplatin is given. Response to chemotherapy is assessed by CT scan and repeated estimation of the tumour marker CA-125 in case of malignant nonmucinous epithelial tumours. When the disease recurs second-line drugs can be given as topotecan and liposomal.

3. Radiotherapy

It is no more used in the routine management of ovarian carcinoma. Whole abdominal irradiation leads to acute and chronic intestinal obstruction in about 30% of cases, and will need laparotomy with its complications. So radiotherapy has been replaced by chemotherapy except in patients who refuse or are not good candidates for chemotherapy.

Interval (Intervention) Debulking Operation (Secondary Cytoreduction)

It is performed in advanced ovarian cancer, when the primary surgery is incomplete, and residual tumour masses are left behind. Three courses of chemotherapy are given, followed by laparotomy to remove the residual lesions. Chemotherapy is then continued after the surgery. The survival rate at 3 years is increased by up to 20%.

Note for the postgraduate

Second-look operation. Laparotomy is carried out in a patient who has a clinical and radiological cure, and a normal serum level of tumour marker after receiving a complete course of chemotherapy. After laparotomy, peritoneal washings are done for cytological examination. This is followed by full exploration of the pelvis and abdomen, then multiple random peritoneal biopsies are taken to exclude microscopic metastases. The procedure does not improve the prognosis and is no more done.

PROGNOSIS

The 5-year survival rate is:

- Stage I 80-90%
- Stage II 60-70%
- Stage III 15-30%
- Stage IV 5-15%

The overall 5-year survival rate is poor, about 30%.

Notes for the postgraduate

- Carboplatin has less nephrotoxicity, neurotoxicity, and ototoxicity compared with cisplatin. However, it causes more suppression of the bone marrow.
- The dose of paclitaxel (Taxol) is 135 or 175 mg/m² given IV over 3 or 24 hours and repeated every 3 weeks.
- The dose of cisplatin (Platinol) is 75 mg/m² I.V. for one day and repeated every 3 weeks.
- Progestational agents can be used for recurrent well-differentiated endometrioid carcinoma which is positive for oestrogen receptors.
- Dysgerminoma is the commonest ovarian cancer occurring in pregnancy. It is very radio-sensitive, but still chemotherapy is preferred when adjuvant therapy is needed.
- A tumour mass of 1 cm in diameter contains about one billion malignant cells.
- Epithelial tumours may be benign, borderline or malignant. Borderline tumours show malignant changes in the epithelial cells, but there is no stromal invasion. These tumours are benign in the majority of cases, however, about 15% become locally invasive, and may metastasize. They are treated by surgery alone, and adjuvant chemotherapy is of no value.
- The palpable ovary syndrome. The diameters of the postmenopausal ovary are 0.5 x 1 x 1.5 cm rendering it impalpable on bimanual examination. Any ovary palpable 3 or more years after menopause is considered pathological and indicates investigations.

GENERAL REMARKS

Ovarian Tumours Occurring during Childhood

1. Germ cell tumours.
2. Granulosa cell tumour.

Teratoma is the commonest ovarian tumour in children.

Functioning Ovarian Tumours

1. Feminizing (oestrogenic) tumours.
2. Virilizing (androgenic) tumours.
3. Gynandroblastoma.
4. Struma ovarii.
5. Choriocarcinoma of the ovary.
6. Brenner tumour sometimes secretes oestrogen.

Ovarian Tumours Causing Uterine Bleeding

1. Oestrogenic tumours (granulosa and theca cell tumour).
2. Malignant ovarian tumour with uterine metastasis.
3. Twisted ovarian tumour.
4. Brenner tumour as it may secrete oestrogen.

Causes of Postmenopausal Bleeding in a Patient Having an Ovarian Tumour

1. The presence of an oestrogenic tumour.
2. Malignant ovarian tumour with uterine metastasis.
3. Endometrial carcinoma with metastasis in the ovary.
4. Coexisting cancer in the ovary and endometrium.

Ovarian Tumours Causing Amenorrhoea

1. Virilizing (androgenic) tumours. Sertoli cell tumour, Leydig cell tumour, androblastoma, gynandroblastoma, and adrenal-like tumour of the ovary.
2. Cachexia from advanced ovarian malignancy.
3. Bilateral diffuse fibromata.

Solid Ovarian Tumours

1. **Benign tumours.** Brenner tumour, fibroma, benign solid teratoma as chondroma.
2. **Malignant tumours.** Solid carcinoma, sarcoma, solid malignant teratoma, dysgerminoma, secondaries in the ovaries as Krukenberg tumour.
3. **Functioning Tumours.** Feminizing and virilizing tumours.

Malignant Ovarian Tumours

1. Carcinoma.
2. Sarcoma.
3. Germ cell tumours.
4. Granulosa cell tumour. Malignant in about 25% of cases.
5. Androblastoma. About 5% are malignant.

COMPLICATIONS OF OVARIAN TUMOURS

- (1) Torsion. (2) Haemorrhage. (3) Rupture.
(4) Infection. (5) Incarceration. (6) Malignant change.

Torsion

It is the commonest complication. The incidence is about 5% without pregnancy, 10% with pregnancy and 20% during puerperium.

Aetiology

A. Predisposing Factors

1. If the tumour is small or moderate in size because large tumours are difficult to rotate.
2. Long pedicle.
3. Absence of adhesions.

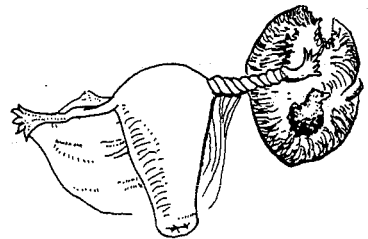


Fig.104. Torsion of ovarian tumour

4. Abdominal tumours rotate easily than pelvic tumours due to the presence of space.
5. Pregnancy as the tumour becomes displaced by the growing uterus.
6. In the puerperium due to laxity of abdominal wall and presence of space.

B. Precipitating Factors

1. Sudden movement of the patient or turning in bed.
2. Movement of the intestine during defaecation specially in diarrhoea.
3. Sudden contraction of abdominal muscles as in coughing.
4. Contraction of uterus during labour.
5. Abdominal massage after delivery.
6. Haemodynamic action. After the initial twist, torsion may be continued as the uterine and ovarian arteries now pulsate in opposite directions.
7. Idiopathic.

Changes which occur in the tumour as a result of torsion

Torsion may be acute or chronic.

- A. Chronic torsion. The veins are occluded at first, because their walls are thin and this leads to: (1) congestion of the tumour; (2) haemorrhage into the tumour due to severe congestion; (3) rupture due to haemorrhage; (4) exudation of lymph occurs on the surface of the tumour leading to adhesions to the omentum or intestine; (5) infection may reach the tumour from the bowel along the adhesions; (6) adhesions may become vascularized and the pedicle may atrophy leading to a parasitic tumour attached to the omentum.
- B. Acute torsion. In rare cases both arteries and veins are occluded causing necrosis of the tumour.

Clinical Picture

Complete torsion leads to sudden onset of severe abdominal or pelvic pain, accompanied with vomiting and a variable degree of shock. Pain usually occurs after a sudden movement of the patient. On examination, the lower abdomen is rigid due to peritoneal irritation and we may feel a tender pelvi-abdominal mass. Low grade fever and leucocytosis may occur. Ultrasonography will reveal a cystic or solid adnexal mass.

With incomplete torsion, the condition is subacute with mild pain and there may be a previous history of similar attacks of pain without significant fever or leucocytosis.

Treatment

It is by ovariectomy (removal of the whole ovary with the tumour).

Note. The degree of torsion varies from a half turn to 12 complete turns which is the maximum record.

Haemorrhage

It may be internal in the tumour or external in the peritoneal cavity.

Aetiology

It occurs as a result of: (1) torsion; (2) direct trauma to the abdomen; (3) obstetric trauma during labour; (4) bimanual examination; (5) malignancy eroding the blood vessels.

Clinical Picture

There is abdominal pain accompanied with a variable degree of shock. The tumour is enlarged and tender.

Treatment

It is by ovariectomy.

Rupture

It is due to the same causes of haemorrhage. In case of malignancy, the malignant tissue fungates through the capsule of the tumour.

The Results of Rupture

These depend upon the contents of the cyst. In simple serous cyst the fluid is not irritant and is soon absorbed. Papillary cyst may lead to implantation of papillae on the peritoneum and ascites. Mucinous cyst may cause myxoma peritonei. The sebaceous material in a dermoid cyst is very irritant and causes chemical peritonitis with dense adhesions. Infected cyst causes septic peritonitis. Malignant cyst causes dissemination of malignancy.

Clinical Picture

Sudden onset of severe abdominal pain accompanied with a variable degree of shock. However, rupture of a small cyst may be symptomless or causes momentary pain or discomfort. On examination the cyst disappears if unilocular, or becomes changed in shape if multilocular. There may be evidence of free fluid or blood in the peritoneal cavity. Further symptoms depend upon the contents of the cyst.

Treatment

Ovariectomy and peritoneal toilet.

Infection

Aetiology

It occurs in the following conditions: (1) after torsion as a result of adhesions to the bowel; (2) spread from an adherent infected organ as in case of appendicitis or diverticulitis; (3) ascending infection after abortion or labour; (4) infection by the bloodstream.

Clinical Picture

Abdominal pain, fever and sometimes vomiting. The tumour is tender, fixed and increases in size. There is leucocytosis and high sedimentation rate.

Treatment

Antibiotics and ovariectomy. If extensive adhesions prevent removal of the cyst we do marsupialization, where the wall of the cyst is sutured to the parietal peritoneum followed by drainage with a rubber tube which is left until no more fluid is obtained.

Incarceration

An ovarian tumour may become incarcerated in Douglas pouch due to adhesions, projecting sacral promontory or simple impaction. It causes pelvic pain and pressure symptoms in the form of dysuria, dyschezia, and dyspareunia. Treated by surgical removal which may be difficult due to the presence of adhesions.

Malignant Change

The clinical signs suggesting malignancy have been mentioned before. Any ovarian tumour removed must be examined histologically to exclude malignancy. The treatment is total hysterectomy and bilateral salpingo-oophorectomy with omentectomy and appendectomy. This is followed by chemotherapy.

TYPES OF OVARIAN CYSTS

1. Retention Cysts

- a. Follicular cyst(s): Due to failure of rupture of the graafian follicle which continues to grow to form a cyst; found in cases of metropathia haemorrhagica, polycystic ovary syndrome, sometimes with fibroids and as a result of treatment with clomiphene or gonadotrophins. A retention cyst never exceeds 5 cm. in diameter and will decrease in size or disappear within 2 months.
- b. Lutein cysts: Lined by granulosa lutein or theca lutein cells or both. The change is usually marked in the theca cells when the term theca lutein cyst is used. Luteinization means the cells become distended with fluid rich in cholesterol, phospholipids and contains carotene pigment which gives a yellow colour. Found in cases of hydatidiform mole and choriocarcinoma. Another example is a persistent corpus luteum which grows for a time forming a cyst. This leads to a short period of amenorrhoea followed by bleeding when it degenerates.

2. Inflammatory Cysts

Ovarian abscess, tubo-ovarian cyst and tubo-ovarian abscess.

3. Chocolate Cysts

These are due to endometriosis. Rarely exceed 10 cm in diameter, and may be bilateral.

4. Cystic Neoplasms

These may be benign or malignant. Examples include simple serous cyst, papillary serous cystadenoma, mucinous cystadenoma and dermoid cyst. Malignant cystic tumours as papillary serous cystadenocarcinoma, mucinous cystadenocarcinoma and malignant change in a dermoid cyst.

5. Walthard Inclusion Cysts

The surface epithelium covering the ovary may grow downwards into the substance of the ovary and form microscopic cysts. These inclusions may remain quiescent or form tumours of epithelial origin as cystadenomas.

PARAOVARIAN (BROAD LIGAMENT) CYST

It is due to cystic dilatation of the embryonic remnants of the Wolffian system found between the 2 layers of the broad ligament. The cyst is thin walled, unilocular and lined by flat epithelium. It contains serous fluid and never becomes malignant. It causes stretching of the fallopian tube. The cyst is fixed and pushes the uterus to the opposite side. Stretching of the tube can be shown by hysterosalpingography. These points differentiate it from an ovarian cyst. The cyst can attain a large size filling the whole abdominal cavity. It is treated by surgical removal after incising the peritoneum of the broad ligament.

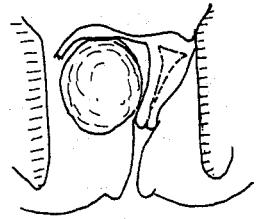


Fig.105. Paraovarian cyst

SECTION X

MISCELLANEOUS

TUMOUR MARKERS

The tumour marker is a substance produced by tumour cells and its concentration is measured in serum to help diagnosis, to assess the tumour response to treatment and to detect recurrence. Tumour markers include the following four groups:

I. FETAL PROTEINS (ONCOFETAL ANTIGENS)

These are antigens produced by fetal tissues and tumours.

- A. Alpha-fetoprotein. It is a glycoprotein produced by fetal liver, upper gastrointestinal tract and yolk sac. It is produced by germ cell tumours containing yolk sac elements as endodermal sinus tumour and embryonal carcinoma of the ovary which is a mixture of endodermal sinus tumour and choriocarcinoma. It is also produced by hepatocellular carcinoma and occasionally by carcinoma of the stomach, pancreas, and biliary system. Normal level is 0-10 nanograms/ml.
- B. Carcinoembryonic antigen (CEA). It is a protein produced by embryonic tissues. It is also produced by benign and malignant lesions of the gastrointestinal tract, mucinous carcinoma of the ovary, endometrial carcinoma and adenocarcinoma of the cervix. Normal level is 0-4 nanograms/ml. Elevated in smokers.

II. HORMONES

- A. Human chorionic gonadotrophin (HCG). It is a valuable marker for gestational trophoblastic tumours, ovarian choriocarcinoma, embryonal carcinoma and malignant teratomas containing trophoblastic tissue. Embryonal carcinoma produces both alpha-fetoprotein and HCG.
- B. Inhibin. It is a glycoprotein produced by granulosa cells of the ovary. Its function is to inhibit the release of follicle stimulating hormone (FSH). Elevated levels are seen in most granulosa cell tumours, and it is useful to monitor these tumours. Normal level is 22-50 picograms/ml.

III. ENZYMES

- A. Placental Alkaline Phosphatase. Serum level is raised in most patients with ovarian carcinoma particularly germ cell tumours as dysgerminoma. Also raised in patients with breast, lung, and gastric carcinoma, and other benign conditions as hepatitis and colitis and a high number of smokers.
- B. Lactic acid dehydrogenase. It is raised in dysgerminoma.

IV. TUMOURS ASSOCIATED ANTIGENS

These are glycoproteins present on the surface of malignant cells but not on similar benign cells. These antigens are acquired during the malignant transformation of the cell and the cause is unknown. Patients with malignant epithelial tumours of the ovary have elevated serum levels of CA-125 (cancer antigen-125), CA-19-9, OCA (ovarian cancer antigen) and OCCA (ovarian cystadenocarcinoma antigen). The normal value of CA-125 is 0-35 U/ml.

CA-125 is derived from coelomic and müllerian duct epithelium, so it increases (>35 U/ml) in benign and malignant conditions derived from these structures. It is detected by radioimmunoassay and its serum level is increased in the following conditions:

1. About 80% of patients with nonmucinous epithelial carcinoma of the ovary. So a normal level does not exclude cancer.
2. Adenocarcinoma of the fallopian tube, endometrium, and endocervix.
3. Endometriosis.
4. Fibroids.
5. Carcinoma of breast, lung, colon, and pancreas.
6. Pelvic inflammatory disease.
7. First trimester of normal pregnancy. It is derived from the decidua.
8. Postoperative to gynaecologic surgery.
9. Hepatic cirrhosis and renal failure.
10. 1% of normal healthy women show a level above 35 U/ml.

CA-19-9 is raised in mucinous ovarian carcinoma (normal value 0-37 U/ml). OCA and OCCA are raised in both serous and mucinous ovarian carcinoma.

Tumour Markers Useful in The Management of Ovarian Cancer

Tumour Marker	Types of Tumour Identified
CA -125	Nonmucinous epithelial ovarian carcinoma
CA -19-9	Mucinous epithelial ovarian carcinoma
Carcinoembryonic antigen	Mucinous epithelial ovarian carcinoma
Alpha-fetoprotein	Endodermal sinus tumour Embryonal cell carcinoma
HCG	Embryonal cell carcinoma Ovarian Choriocarcinoma Mixed germ cell tumours
Placental alkaline phosphatase and lactic acid dehydrogenase	Dysgerminoma

Tumour Markers for Endometrial Carcinoma

- CA -125.
- CEA.

Tumour Markers for Cervical Carcinoma

- CEA for adenocarcinoma.
- SCCA (Squamous cell carcinoma antigen) and TA-4 (tumour antigen-4) for squamous cell carcinoma.

SEXUAL DISORDERS

I. DYSPAREUNIA

It means difficult or painful coitus.

AETIOLOGY

1. Lesions in the vulva. Vulvitis, bartholinitis, urethral caruncle and painful episiotomy scar.
2. Lesions in the vagina. Vaginitis, ulcers, tumours, septa, tender scar, short vagina, stenosis, disproportion between the male and female organs, thick rigid hymen, first coitus due to rupture of the hymen, vaginismus and dryness of the vaginal orifice due to deficient secretion of Bartholin glands. Vaginismus is the commonest cause of dyspareunia.
3. Congenital elongation of cervix, acute or chronic cervicitis if infection has caused parametritis.
4. Retroversion due to direct pressure on the uterus.
5. Chronic salpingo-oophoritis due to the presence of tender inflammatory swellings in Douglas pouch.
6. Prolapse of ovaries in Douglas pouch.
7. Parametritis.
8. Pelvic endometriosis or endometriosis of the rectovaginal septum.
9. Mass in Douglas pouch as ovarian cyst, fibroid and pelvic haematocèle.
10. Extragenital lesions as urethritis, cystitis and anal fissure.
11. Ignorance of the husband.

Classification

1. External or superficial dyspareunia. Pain occurs during penetration and is due to lesions in the vulva, vagina and extragenital lesions.
2. Internal or deep dyspareunia. Pain occurs after complete penetration and is due to deep lesions (causes 3-9).

TREATMENT

It is the treatment of the cause.

II. VAGINISMUS

DEFINITION

It is reflex spasm of the vaginal sphincter and levator ani muscles on any attempt at sexual intercourse or vaginal examination. In severe cases it is accompanied by spasm of the gluteal and adductor muscles of the thighs.

Note. The vaginal sphincter is made by the 2 bulbocavernosus muscles.

TYPES

- A. Primary vaginismus. No local abnormality is found and it is due to psychological disturbances, and may be related to sexual trauma or abuse.
- B. Secondary vaginismus. It is due to painful coitus, so it is a protective reaction.

TREATMENT

A. Primary Vaginismus

1. Psychotherapy and sexual education.
2. Gradual dilatation of the vagina may be needed. Dilators are used by the patient or husband. Dilatation is done once or twice daily and the dilator is left in position for 10-15 minutes on each occasion until the largest dilator can be passed before coitus is attempted.
3. Occasionally, manual dilatation of the vagina under general anaesthesia is done, or a mediolateral or midline episiotomy is performed and resutured transversely to widen the vagina (Fenton operation).

B. Secondary Vaginismus

It is dealt with by treating the cause.

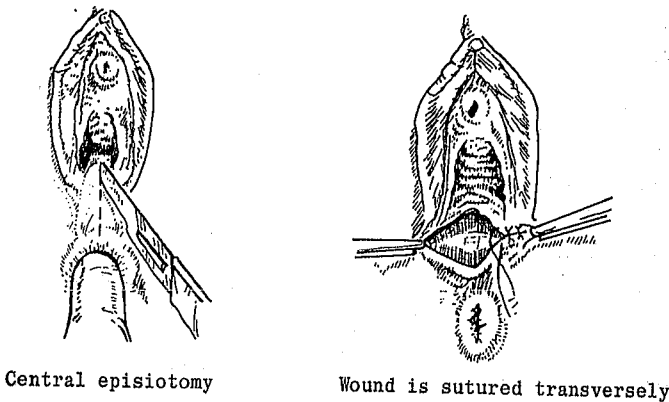


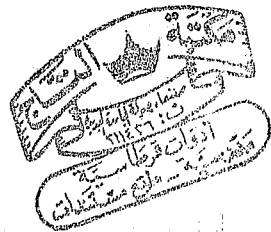
Fig. 106. Fenton operation

III. FRIGIDITY

It is absence of sexual desire (libido).

AETIOLOGY

1. Physiological. Before puberty, after menopause, during pregnancy and for a variable time after delivery.
2. Constitutional. Women have different appetites for coitus as they have for food, music and games and nothing can alter this.



3. Psychological. Wrong ideas about sex and intercourse.
4. Lack of love for the husband.
5. Fear of pregnancy and childbirth.
6. The presence of dyspareunia from any cause.
7. Contraceptive pills may reduce libido.
8. Long-standing infertility; coitus becomes a purposeless job.
9. Endocrine diseases. Diabetes mellitus, thyroid dysfunction and adrenal hypofunction.
10. Hyperprolactinaemia
11. Female circumcision which is still practiced in some communities.
12. Ill-health and physical fatigue.

TREATMENT

1. Education and explanation.
2. Treatment of the cause as diabetes mellitus, and hyperprolactinaemia.
3. Small doses of methyltestosterone, 5 mg once or twice daily for a few weeks or small doses of corticosteroids.

Note. Increased sexual desire in female is called nymphomania, and in male is called satyriasis. Hypersexuality is treated by (a) psychotherapy; (b) the antiandrogen cyproterone acetate (Androcur) 50 mg b.i.d.

INTERSEX

It is incomplete sexual differentiation into either male or female.

AETIOLOGY

1. Chromosomal abnormalities (Chromosomal Intersex)

- a. **Turner syndrome.** The individual is a female with 45 chromosomes (45XO).
- b. **Klinefelter syndrome.** The individual is a male with an extra X chromosome, so the karyotype is 47,XXY. Some patients have more than 2 X chromosomes, and some have a mosaic karyotype (47,XXY-46,XY). The extra X chromosome may lead to somatic abnormalities as gynaecomastia (90%), female distribution of pubic hair, and mental retardation which increases with the increase in number of X chromosomes. The penis and testicles are small. There is hyalinization of the seminiferous tubules leading to azoospermia or the production of few sperms leading to infertility. However, the mosaic individual may be fertile.
- c. **The triple X syndrome.** The individual is a female with 47 or 48 chromosomes (47XXX) or (48XXXX).
- d. **The YY syndrome.** The individual is a male with 47XYY, or 48XXYY. He is usually taller than normal and mentally retarded.
- e. **Mixed gonadal dysgenesis.** The individual is a female. The karyotype is mosaic; 45XO/46XY. There is one testis on one side and a streak gonad or no gonad on the other side. The external genital organs may be ambiguous, and the patient virilizes at puberty. Gonadectomy is indicated to remove the source of androgens and to avoid the risk of malignancy.

2. Gonadal Abnormalities (Gonadal Intersex)

- a. **The true hermaphrodite.** The individual has both testicular and ovarian tissues in different combinations. An ovary on one side and a testis on the other side, or an ovary or testis on one side and an ovotestis on the other side, or an ovotestis on both sides. The sex chromosomes may be male (XY) or female (XX) or mosaic, i.e. some cells are XX and others are XY. However, true hermaphrodites are commonly XX. The external appearance (phenotype) may be male or female. The external genital organs may be male or female or ambiguous. Diagnosis is made by gonadal biopsy.
- b. **Pure gonadal dysgenesis.** The gonads are in the form of fibrous bands (streak gonads). The external appearance is female. The internal and external genital organs are female but remain infantile due to absence of gonads. The chromosomal arrangement (karyotype) is 46XX or 46XY. When the karyotype is 46XY, the condition is termed Swyer syndrome.
- c. **Sex inversion.** The external appearance is a male with testes but the chromosomes are 46 XX, so there is sex inversion or deviation between chromosomal and gonadal constitution.

3. Hormonal Disturbances

- a. **Congenital Adrenal Hyperplasia (CAH).** It is due to failure of synthesis of cortisol from 17α -hydroxyprogesterone due to deficiency of certain enzymes mostly 21-hydroxylase enzyme (95%) and occasionally 11 beta-hydroxylase. Failure to produce cortisol leads to increased production of ACTH, which leads to hyperplasia of the adrenal cortex and increased production of androgens from 17α -hydroxyprogesterone. There is virilization of the female fetus with enlargement of the clitoris, fusion of labia minora, and hirsutism. The fallopian tubes, uterus, and vagina are present but remain infantile. The uterus fails to menstruate causing amenorrhoea. About 75% of infants have hyponatraemia and hyperkalaemia (salt-losing), due to decreased synthesis of aldosterone. Treatment is by prednisolone or dexamethasone for life to suppress ACTH production. Dose is adjusted by the level of 17α -hydroxyprogesterone. Surgical correction of the external genitalia is carried out, preferably during the first 2 years of life to avoid psychological injury of the child. Normal sexual and reproductive function can occur with proper medical treatment. Children born to a patient with CAH are examined properly as the condition is inherited as autosomal recessive disorder from the mother or father (1 in 200).

Note. The internal genital organs are differentiated by the tenth week of pregnancy, while the adrenal cortex does not function before the twelfth week. This explains the presence of fallopian tubes, uterus, and vagina. They remain infantile because of androgens secreted after twelfth week.

- b. **Virilization of the female fetus** may occur if the pregnant mother has a virilizing ovarian tumour or receives androgens or progestogens during pregnancy.

4. End-organ Resistance

An example is testicular feminization (complete androgen insensitivity syndrome).

5. Psychological Intersex

- a. **Homosexuality.** The person is attracted to the same sex.
b. **Transvestism.** The person has a desire to wear the clothes of the opposite sex.
c. **Transsexuality.** It is the desire to change sex by operation.

INVESTIGATION OF INTERSEXUALITY

1. **Buccal smear.** If two X chromosomes are present, a chromatin mass or Barr body will be seen beneath the nuclear membrane of the cell, so the female cell is chromatin positive while the male cell is chromatin negative (the Barr body is present in 20-50 per cent of the female epithelial cells).
2. **Examination of neutrophils.** The chromatin mass gives a "drum stick" appearance to one of the lobes of the nucleus. It is present in 20% of the neutrophils of the female subject.

3. Chromosomal culture. Skin, blood or bone marrow is cultured by special methods to determine the number and shape of chromosomes.
4. Hormonal estimations in blood and urine.
5. Examination of internal genital organs by ultrasound, laparoscopy and laparotomy. Histological examination of the gonad is decisive.
6. CT scan or MRI of the sella turcica and adrenal gland to diagnose a tumour.

N.B.:

- Pseudohermaphroditism means the gonads belong to one sex and the external genital organs belong to the other sex. If the gonads are ovaries the individual is a female pseudohermaphrodite, e.g. congenital adrenal hyperplasia. If the gonads are testes the individual is a male pseudohermaphrodite, e.g. testicular feminization syndrome.
- Mosaicism is diagnosed if more than 5% of cells show normal karyotype.
- The chosen sex of rearing is determined, then the gonadal tissue which is not appropriate to the chosen sex is removed.

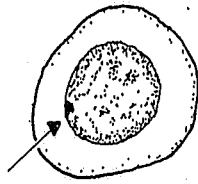


Fig.107. Barr body

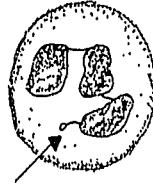


Fig.108. Drumstick appearance



HIRSUTISM

DEFINITION

It is excessive growth of terminal hair in abnormal sites, i.e. in a male-like pattern. The eleven abnormal sites include the upper lip, beard, chest, upper abdomen, lower abdomen, upper back, lower back, arms, forearms, thighs, and legs.

Note. Terminal hair is the thick dark pigmented hair. Vellous hair is the thin pale nonpigmented hair.

FACTORS RESPONSIBLE FOR HIRSUTISM

1. Increased level of serum androgen due to:
 - a. Increased androgen production from the adrenal glands.
 - b. Increased androgen production from the ovaries.
 - c. Exogenous androgens.
 - d. Decreased production of sex-hormone binding globulin (SHBG). This leads to increased amount of free testosterone. About 80% of circulating testosterone is bound to SHBG, 19% to albumin, and 1% is free. Free testosterone is the biologically active testosterone.
2. Increased sensitivity of hair follicles to normal amounts of testosterone.

Sex-hormone binding globulin

It is formed in the liver. Oestrogens, pregnancy, and hyperthyroidism increase the biosynthesis of SHBG. Androgens, hypothyroidism, obesity, insulin, prolactin and growth hormone (acromegaly) decrease the SHBG and thus increase the free testosterone.

Androgen production

Androgens are produced by the ovaries and adrenal glands.

Testosterone. 25% produced by the ovaries, 25% by the adrenal glands, and 50% result from peripheral conversion of androstenedione. This occurs mainly in body fat, but also in the liver, skin, and muscles.

Androstenedione. 50% from the ovaries, and 50% from the adrenal glands.

Dehydroepiandrosterone (DHEA). 10% from the ovaries and 90% from adrenal glands.

Dehydroepiandrosterone sulphate (DHEAS). Almost 100% from adrenal glands.

The normal serum testosterone level in the female is 0.2-0.8 nanogram/ml, i.e. less than 1 ng/ml.

AETIOLOGY

1. Constitutional, idiopathic, or familial hirsutism. This is the commonest cause (90%). There is a familial and racial incidence. It is more among Mediterranean than among Asian people. It is due to increased sensitivity of hair follicles to normal amounts of testosterone or increased conversion of testosterone to dihydrotestosterone caused by increased activity of 5 alpha-reductase enzyme. Dihydrotestosterone is the hormone which

stimulates the hair follicles. The menstrual cycles are regular and circulating androgens have normal levels.

2. Ovarian causes. The polycystic ovary syndrome (PCO), virilizing ovarian tumours, stromal hyperplasia, stromal hyperthecosis, pregnancy luteoma, and hyperreactio luteinalis.
3. Adrenal causes. Congenital and adult-onset adrenal hyperplasia, and Cushing syndrome.
4. Pituitary causes. (a) Cushing disease due to basophil adenoma with increased production of ACTH and secondary adrenal hyperplasia; (b) acromegaly; SHBG production is decreased; (c) prolactinoma.
5. Juvenile myxoedema. Hypothyroidism decreases the biosynthesis of SHBG.
6. Hyperprolactinaemia. Prolactin increases the production of adrenal androgens and decreases the biosynthesis of SHBG.
7. Hirsutism may develop for the first time during pregnancy.
8. After the menopause.
9. Iatrogenic. This may occur during treatment with drugs as androgen, anabolic drugs, danazol, ACTH and some progestogens, e.g. norethisterone.

Notes for the postgraduate

- Idiopathic hirsutism and PCO syndrome account for 95% of cases of hirsutism.
- Stromal hyperplasia. There is non-neoplastic proliferation of the ovarian stromal cells. The cells produce androgens.
- Stromal hyperthecosis. There is proliferation of ovarian stroma with areas of hyperplasia and luteinization of theca interna cells. It is bilateral and both ovaries are enlarged to reach a diameter of 5-7 cm. Theca cells produce androgens.
- Virilism means the presence of hirsutism plus one or more of the following: temporal baldness, hoarseness (deepening) of voice, atrophy of the breasts, hypertrophy of the clitoris, and increased muscle mass. Virilism is due to excessive androgenic stimulation which is usually caused by congenital adrenal hyperplasia and ovarian or adrenal tumour.
- Luteoma of pregnancy. It is due to excessive luteinization of the theca cells of the ovary resulting from exaggerated response to normal level of HCG which acts like I.H. The luteoma forms a solid nodule of lutein cells. It is often multifocal and affects both ovaries and can reach 20 cm in diameter. It produces androstenedione leading to maternal virilization as well as abnormal genitalia in the female fetus. However, it is not removed as it undergoes spontaneous regression after delivery.
- Hyperreactio luteinalis. The lesion which also occurs only during pregnancy takes the form of multiple cystic tumours in both ovaries with increased production of androgens leading to maternal virilization in the form of hirsutism and clitoromegaly, however, the fetus is not affected. In most cases the serum HCG is very high. Also the lesion disappears spontaneously after delivery. This lesion and pregnancy luteoma are responsible for hirsutism during pregnancy.
- Some progestogens have androgenic effect by (a) direct stimulation of testosterone receptors and (b) displacing testosterone from SHBG to increase the free testosterone.

DIAGNOSIS

A. History

Ask about the following points:

- Age at onset of hirsutism.
- Rate of progression (rapid with a tumour).



- Menstrual history and any abnormality as amenorrhoea or oligomenorrhoea.
- Change in weight.
- Family history of hirsutism.
- History of galactorrhoea.
- History of drug intake.

B. Physical Examination

- Areas involved.
- Signs of virilism.
- Breast examination for atrophy and galactorrhoea.
- Signs of Cushing syndrome, congenital adrenal hyperplasia, acromegaly, and thyroid disease.
- Presence of abdominal mass (adrenal tumour).
- Pelvic examination for clitoromegaly (clitoral index more than 35 mm^2), polycystic ovaries, and ovarian tumour.

Note. Clitoral index = Sagittal diameter of clitoris $\times$ transverse diameter. Normally $<35 \text{ mm}^2$.

C. Investigations

Measure serum testosterone. If normal i.e. less than 1 ng/ml no further investigation is needed and the case is diagnosed as idiopathic hirsutism. It is preferable to measure the total and free testosterone. If serum testosterone is high, the following is done:

1. Check serum FSH, LH and prolactin. Increased LH and LH:FSH ratio 2 or more diagnose PCO syndrome. Serum prolactin to exclude hyperprolactinaemia.
2. To diagnose Cushing syndrome, measure serum or 24 hour urinary cortisol and serum DHEAS. If there is increased activity of the suprarenal cortex, do the dexamethasone suppression test to exclude the presence of a tumour.
3. If congenital or adult-onset adrenal hyperplasia is suspected, measure the serum 17α -hydroxyprogesterone (more than 8 ng/ml is diagnostic).
4. Thyroid function tests to exclude hypothyroidism (TSH, T3, and T4).
5. Ultrasonography. It confirms the diagnosis of PCO syndrome, and excludes the presence of ovarian or adrenal tumour.
6. CT scan and MRI to diagnose pituitary or adrenal tumour.
7. If the testosterone level is high and the ovaries and adrenal glands are normal on scan, direct catheterization of ovarian or adrenal vein may be done to know the source of increased androgen.

Notes for the postgraduate

- Nanogram = millimicrogram = one billionth of a gram.
- Dexamethasone suppression test. One milligram dexamethasone is given orally at 11 pm and blood sample is taken next morning at 8 am for serum cortisol. A value less than $5 \text{ micrograms/100 ml}$ excludes Cushing syndrome (caused by adenoma or carcinoma of suprarenal cortex and the production of cortisol by tumour cells is not affected by ACTH).

- Urinary 17-Ketosteroids are metabolites of adrenal androgens except testosterone. Their estimation is replaced by estimation of serum DHEAS.
- Adult-onset adrenal hyperplasia is due to mild deficiency of 21-hydroxylase enzyme. At birth the external genital organs are normal (no virilization) but signs of androgen excess appears after puberty leading to amenorrhoea, hirsutism, and clitoromegaly.
- Serum testosterone more than 2 ng/ml indicates ovarian or adrenal tumour.

TREATMENT

A. Treatment of the Cause

Examples include removal of an androgenic ovarian or adrenal tumour and corticosteroids for congenital adrenal hyperplasia (prednisolone 7.5-10 mg daily in divided doses).

B. Treatment of Idiopathic Hirsutism

1. Cosmetic Treatment

Hair is removed by shaving, depilatory creams, bleaching, waxing, laser, or electrolysis. The latter affords effective and permanent relief but is expensive, time-consuming and may cause pigmentation. Also obese women should lose weight.

2. The Combined Contraceptive Tablet

Oestrogen increases the synthesis of SHBG and decreases free testosterone. Oestrogen also reduces the conversion of testosterone to dihydrotestosterone by inhibiting 5 α -reductase enzyme. The progestogen inhibits LH secretion and so androgen production by the ovary is reduced. However, some of the progestogens have androgenic effect and so we use a nonandrogenic progestogen. One satisfactory preparation is Diane-35 which has a weak androgenic action. Also the new combined tablets which contain third-generation progestogens as Marvelon and Gynera can be used. The response to treatment is slow and may be 6-9 months before improvement occurs as the hair life cycle is slow. Treatment is given for at least one year and sometimes two years. If oral contraceptive pills are contraindicated or produced side effects we give oral or IM medroxyprogesterone acetate. The oral dose is 10-30 mg daily (Provera tablets) or we give 150 mg IM (Depo-Provera) every 3 months (non-androgenic progestogen).

3. Dexamethasone

It suppresses the adrenal gland and is given if the patient has a high level of DHEAS. The dose is 0.25 mg in the morning and 0.5 mg in the evening. It can be combined with an oral contraceptive pill when only an evening dose is given (0.5 or 0.25 mg) to inhibit the peak activity of ACTH during sleep (early morning).

4. Cyproterone Acetate (Androcur)

It is a progestogen and so inhibits LH secretion, it blocks the androgen receptors in target organs (antiandrogen), it inhibits 5 α -reductase enzyme, and may also suppress ACTH production. The drug is expensive. Side effects include nausea vomiting, weight gain, breast

tenderness, irregular uterine bleeding, decreased libido, and depression. It is also teratogenic during pregnancy as it causes feminization of the male fetus (being antiandrogen the external genital organs will develop in the female direction). For this reason it must be used with oestrogen or oral contraceptive pills to prevent pregnancy. It is given for 10 days starting from the 5th day of the cycle (day 5-14). The dose is 50-100 mg/day. Ethinyl oestradiol is given for 20 days (day 5-24) in a dose of 50 micrograms/day. It improves 70% of cases. Treatment is given for at least one year and sometimes two years.

5. Spironolactone (Aldactone)

This diuretic is aldosterone antagonist. It blocks androgen receptors, inhibits 5 α -reductase enzyme and inhibits the ovarian and adrenal biosynthesis of androgens. It may cause polymenorrhoea and transient polyuria and hyperkalaemia. It causes feminization of the male fetus and so pregnancy must be prevented. Dose is 100-200 mg/day, given continuously or for 3 weeks and one week off starting from first day of the cycle. It is not effective in all cases, and the response is slow

6. Flutamide (Eulexin)

It is antiandrogen as it blocks androgen receptors, so pregnancy must be prevented. Dose is 250 mg (one capsule) daily. Side effects include nausea, vomiting, elevated liver enzymes in addition to galactorrhoea and breast enlargement which occur in 40% of patients.

7. Finasteride (Proscar)

It inhibits 5 α -reductase enzyme and so pregnancy must be avoided. Dose is 5 mg (one tablet) daily. It is also used to treat prostate cancer.

8. Gonadotrophin releasing hormone analogues (agonists)

These inhibit the production of oestrogens and androgens from the ovary and lead to amenorrhoea. Side effects include hot flushes, dry vagina and dyspareunia. Osteoporosis occurs if given for more than 6 months, so for prolonged therapy we add oestrogen and a progestogen (add-back therapy).

9. Insulin Sensitizing Agents

Some oral hypoglycaemics as metformin are used in PCOS. The drug reduces hyperinsulinaemia which leads to hyperandrogenism.

Notes for the postgraduate

- Hirsutism in pregnancy. Human chorionic gonadotrophin (HCG) acts like LH and stimulates the theca cells of the ovary to produce androgens. In some cases the response of the theca cells to HCG is exaggerated leading to formation of pregnancy luteoma.
- Hirsutism after the menopause. Oestrogen production is decreased leading to decreased synthesis of SHBG and so free testosterone is increased.
- Hirsutism associated with obesity. There is increased conversion of androstenedione into oestrone in fatty tissue. Oestrone stimulates the secretion of LH. Obesity also reduces the synthesis of SHBG and so free testosterone is increased.

URINARY SYMPTOMS

I. FREQUENCY OF MICTURITION

AETIOLOGY

1. Lesions in the urinary tract as urethritis, cystitis, calculi and tumours.
2. Abnormalities of urine:
 - a. Excessive amount in diabetes mellitus or insipidus and impaired renal function.
 - b. Excessive acidity as in *E. coli* infection.
 - c. High concentration of oxalate, phosphate or urate salts.
3. Habit and psychological disturbances.
4. Cold environment.
5. Gynaecological lesions:
 - a. Cystocele.
 - b. Infection of the genital tract as vaginitis, cervicitis and salpingitis through spread of infection to the bladder by lymphatics.
 - c. Painful lesion in the vulva as acute vulvitis may cause reflex frequency of micturition.
 - d. Pelvic tumour pressing on the bladder as fibroid, or ovarian cyst.
6. Pregnancy. Pressure on the bladder by the pregnant uterus in the first trimester of pregnancy and by the fetal head after engagement in late pregnancy.

II. RETENTION OF URINE

AETIOLOGY

A. Mechanical Causes

1. Lesions in the urinary tract as stricture, stone or tumour in the urethra or bladder neck.
2. Vagina. Fetal head during labour, haematocolpos or tight pack.
3. Cervix. Large cervical fibroid.
4. Uterus. Incarcerated retroverted gravid uterus or a posterior wall fibroid impacted in Douglas pouch.
5. Ovary. Ovarian tumour impacted in Douglas pouch.
6. Pelvic haematocoele or abscess.

B. Nervous Causes

1. Hysteria.
2. Organic nervous diseases as traumatic paraplegia.
3. Postoperative retention of urine is common. Painful lesion in the abdominal wall, vagina or perineum as episiotomy wound causing reflex spasm of the internal urethral sphincter.

TREATMENT

The bladder is evacuated using a rubber or a plastic catheter, and the cause of retention is treated. The bladder must be evacuated slowly. Rapid emptying will lead to sudden flow of

blood in the mucosal blood capillaries which were compressed by the high intravesical pressure and this may cause rupture of capillaries and haemorrhage.

Note. Catheterization of the bladder for any cause introduces infection in about 2% of cases.

III. INCONTINENCE OF URINE

It is involuntary escape of urine.

TYPES

1. **True incontinence.** In this case, urine escapes continuously by day and by night. It is caused by: (a) urinary fistulae as vesicovaginal fistula; (b) ectopia vesica.
2. **False incontinence (ischuria paradoxa).** It is chronic retention with overflow, urine dribbles from the distended bladder. It may occur with organic nervous diseases as traumatic paraplegia.
3. **Stress urinary incontinence.** It is the commonest cause of urinary leakage.
4. **Urgency incontinence (precipitancy—detrusor overactivity, detrusor instability).** The woman feels the desire to micturate but before she reaches the bathroom urine passes involuntarily. It is due to irritability of the bladder muscle and so the patient cannot inhibit it. It is due to emotional disturbance, neurologic diseases, (as multiple sclerosis and Parkinson disease), and bladder diseases as cystitis, stone or tumour. It may also follow operations used for treatment of stress incontinence.
5. **Nocturnal enuresis.**

STRESS URINARY INCONTINENCE (GENUINE STRESS INCONTINENCE)

DEFINITION

It is involuntary escape of few drops of urine with increased intra-abdominal pressure as during straining, sneezing, coughing, laughing ... etc.

PREVALENCE

It ranges between 10% to 60%.

DEGREES OF STRESS INCONTINENCE

- Grade I. Incontinence occurs only with severe stress, such as coughing, sneezing, or jogging.
- Grade II. Incontinence with moderate stress, such as rapid movement or walking up and down stairs.
- Grade III. Incontinence with mild stress, such as standing. The patient is continent in the supine position.

PHYSIOLOGICAL ANATOMY

- The bladder neck and upper third or half of the urethra are above the level of the pelvic floor. With increased intra-abdominal pressure, the pressure is equally transmitted to the bladder and upper urethra and urine will not escape.
- The internal urethral sphincter (= bladder sphincter) is an involuntary muscle which surrounds the bladder neck.
- The external urethral sphincter is a voluntary muscle and surrounds the middle part of the urethra (compressor urethrae muscle). It empties the urethra after the act of micturition, interrupts the flow of urine on desire, and it acts as a secondary defence mechanism against escape of urine.
- At rest the urethra makes an angle of 90-100 degrees with the base of the urinary bladder called the posterior urethrovesical angle. The urethra also makes an angle of less than 30 degrees with the vertical line.
- During micturition the following changes occur:
 1. Descent of the bladder neck with complete loss of the posterior urethrovesical angle (angle becomes 180 degrees).
 2. Opening (funneling) of the bladder neck and upper urethra.
 3. Descent of the urethra leading to increase in the angle between it and vertical line, so the angle becomes more than 30 degrees.

In stress incontinence, one or all of the above changes occur with increased intra-abdominal pressure.

TYPES OF STRESS INCONTINENCE

Type 1. There is complete loss of the posterior urethrovesical angle.

Type 2. There is complete loss of the posterior urethrovesical angle together with increase in the angle between the urethra and vertical line to be more than 30 degrees. This type leads to severe stress incontinence.

AETIOLOGY

It is due to either weakness of the internal urethral sphincter or descent of bladder neck below the level of the pelvic floor (urethral hypermobility); so the causes are:

1. Congenital weakness of the internal urethral sphincter. Seen in the young nullipara.
2. Trauma to the region of the bladder neck due to vaginal delivery or operation. The incidence of stress incontinence increases with parity due to repeated birth trauma. In fact vaginal delivery is the commonest cause of stress incontinence.
3. Menopause. Lack of oestrogen leads to atrophy of bladder neck supports.
4. Pregnancy and continuous administration of oestrogen-progesterone preparation to induce pseudopregnancy state to treat endometriosis. The hormonal imbalance with increased progesterone weakens the internal urethral sphincter.

5. Genital prolapse. If the bladder neck descends below the level of the pelvic floor, the increased intra-abdominal pressure will be transmitted to the bladder and not to the upper urethra leading to escape of urine.
6. Congenital defects as epispadias, short urethra (less than 1 cm), wide bladder neck, and wide separation of symphysis pubis.
7. Organic nervous diseases as multiple sclerosis.

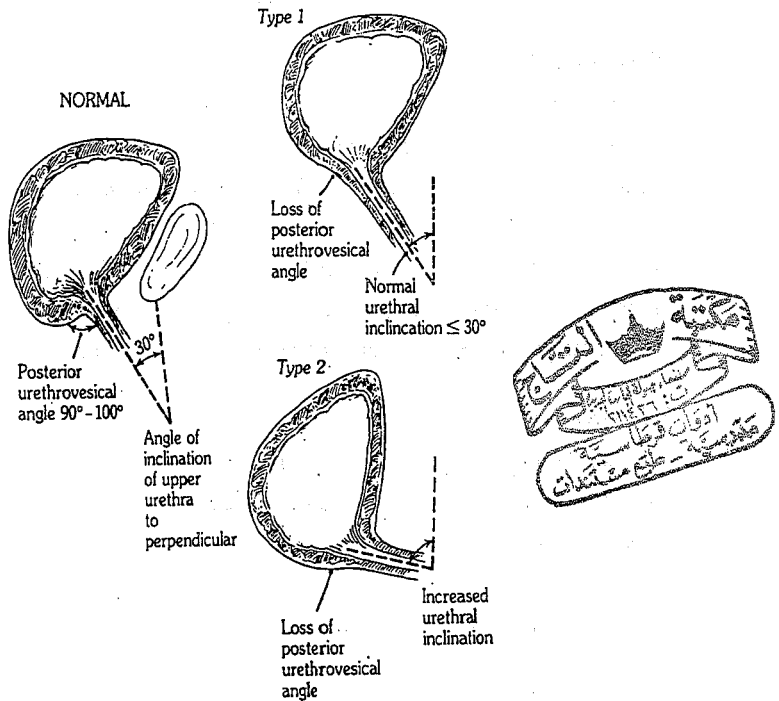


Fig.109. Types of stress incontinence

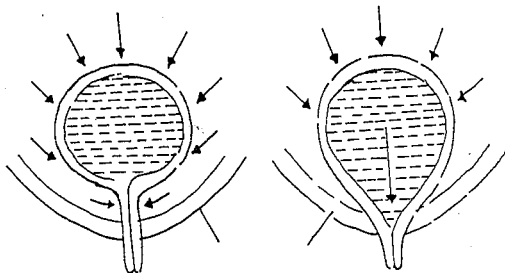


Fig.110. Stress incontinence due to descent of bladder neck

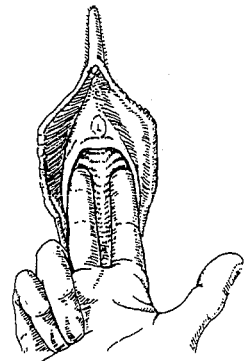


Fig.111. Bonney test

DIAGNOSIS

A. History

1. A detailed history differentiates between the different types of incontinence. Stress incontinence and detrusor overactivity frequently occur together.
2. Gradual onset after menopause suggests oestrogen deficiency.
3. History of vaginal repair or operation in the region of the bladder neck and history of any neurologic disease as multiple sclerosis and Parkinson disease.

B. Diagnostic Tests

1. Stress Test

To diagnose the presence of stress incontinence. The bladder must be moderately full. The patient lies in the lithotomy position, the two labia are separated, and the patient is asked to cough or to strain. If urine escapes from the urethral meatus, the patient is incontinent. If no urine escapes, the test is repeated while the index and middle fingers in the vagina press on the perineum to abolish reflex contraction of the levator ani muscles during straining. If still no urine escapes, the test is repeated while the patient is standing with the legs separated.

2. Bonney Test

It is indicated in case of a positive stress test associated with a cystocele. The aim is to know if incontinence is due to descent of bladder neck or weakness of the sphincter. The index and middle fingers are placed on both sides of the urethra to elevate the bladder neck upwards. If no urine escapes on stress it means that the incontinence is due to descent of the bladder neck, but if urine still escapes it means weakness of the sphincter.

3. Yousef Test

It is indicated in case of a negative stress test associated with a large cystocele to diagnose hidden stress incontinence. The cystocele is reduced, the cervix is grasped with a vulsellum and pushed upward, then the patient is asked to cough. If urine escapes, it indicates that the patient was continent because of kinking of the urethra.

4. Examination of Urine

Urinalysis, culture and sensitivity to exclude cystitis.

5. Cystourethroscopy

To exclude lesions in the urethra and bladder. The bladder neck is examined. It should close in response to straining. However, it opens in case of stress incontinence.

6. Cystourethrography

A radio-opaque dye is injected by a catheter into the bladder. On straining, the lateral view will show absence of the posterior urethrovesical angle in more than 90% of cases. Funneling of the bladder neck in the antero-posterior view may be seen in some cases. The procedure is

recorded on video tape (video cystourethrography) to facilitate diagnosis and for education purposes.

7. Cystometry

To measure the intravesical pressure while the bladder is filled with sterile water or carbon dioxide gas. It diagnoses stress incontinence and detrusor overactivity. The most accurate test to diagnose detrusor overactivity.

8. The Cotton Swab (Q-Tip) Test

Lithotomy position. A sterile applicator with a small piece of cotton at its tip is introduced into the bladder. The swab is pulled back until some resistance is felt. At this point the cotton tip is at the level of the bladder neck. The angle between the applicator and the horizontal is measured. The patient then strains maximally using the Valsalva manoeuvre. This causes descent of the bladder neck and upward movement of the applicator producing a new angle with the horizontal. In normal patients the increase in the angle is less than 30 degrees. In stress incontinence the change is more than 30 degrees indicating poor support and abnormal descent of bladder neck. The test is positive in more than 90% of cases with stress incontinence.

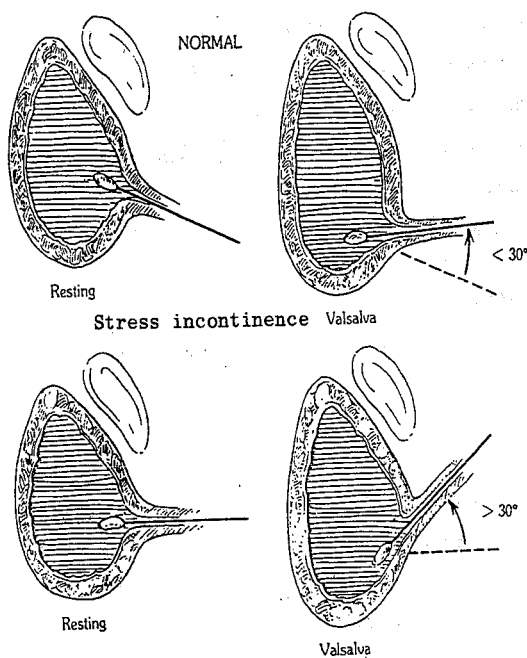


Fig.112. The Q-tip test

9. Measurement of Urethral Pressure

To maintain continence, the urethral pressure (100-120 cm water) must be higher than the intravesical pressure (2-8 cm water). A special catheter is used which measures the intravesical and intra-urethral pressure. The urethral closing pressure equals the intraurethral pressure minus the intravesical pressure (normally 90-100 cm water). The length of the urethra along which urethral pressure exceeds bladder pressure is termed functional length of the urethra which is 3-4 cm. In stress incontinence the urethral closing pressure is reduced.

10. Measurement of Urethral Length

Stress incontinence occurs if the length is less than 1 cm.

11. Uroflowmetry

It records the rate of urine flow through the urethra when the patient is asked to void spontaneously while sitting on uroflow chair. It is used to evaluate patients with stress incontinence before surgery to exclude difficulty in voiding which may be increased by bladder neck surgery. The normal female voids by the rule of "20" – that is urine is passed at a rate of 20 ml/second and the bladder is emptied in less than 20 seconds.

12. Sonography

It gives information about funneling of the bladder neck, both at rest and with Valsalva manoeuvre. It can show bladder or urethral diverticulae. By using three-dimension transvaginal ultrasound, Professor Mahrous showed that continent women have a thick wall internal urethral sphincter which extends from the bladder neck down to the perineal membrane. In stress incontinence, the sphincter is torn as proved by appearance of areas of echolucency. When rupture affects the upper part of the sphincter, the urethra appears "funnel-shaped". When damage affects the lower part, the urethra appears "vase-shaped". When rupture affects the whole length of the sphincter, the urethra appears short and irregular.

13. Electromyography

This is required when neurological dysfunction is suspected.

TREATMENT

I. Prophylactic Treatment

1. During labour, the bladder should be kept empty.
2. Episiotomy is performed if necessary.
3. Physiotherapy. Pelvic floor exercises are started after delivery. These include repeated stoppage of the urinary stream during micturition and repeated contractions of the pelvic floor muscles.

II. Conservative (non-surgical) Treatment

Indications

1. Mild stress incontinence.
2. The patient has not completed her family as vaginal delivery may damage a bladder neck repair.
3. Patient is unfit for surgery or refuses surgery.
4. When stress incontinence is combined with detrusor overactivity. The latter should be treated at first before surgery is done for stress incontinence.

Conservative treatment cures 10% and improves 40% of cases and include:

1. Pelvic floor exercises. Kegel perineometer may be used.
2. Faradic current stimulation of the levator ani muscles to improve their tone.
3. Vaginal cones. A set consists of 5 or 9 cones. Weight ranges from 20 to 100 grams. Patient inserts the cone in the vagina (apex down) and keeps it for 15 minutes twice daily. If this succeeds she inserts the next cone. This improves the tone of the pelvic floor muscles.
4. Oestrogen therapy for menopausal patients. It causes thickening of the urethral mucosa and engorgement of the underlying blood vessels thus increasing the urethral pressure and resistance. It also stimulates the synthesis of collagen by the fibroblasts, and so increases the strength of pelvic connective tissue which supports the pelvic organs. Oestrogen is given orally or as vaginal cream.
5. Alpha-adrenergic stimulants which stimulate contraction of the internal urethral sphincter, e.g. ephedrine.
6. Large vaginal diaphragms, Hodge pessary, and tight fitting tampons to elevate and support the bladder neck.
7. Reduction of weight in obese patients to reduce intra-abdominal pressure.
8. Stop caffeine (to avoid diuresis) and smoking (to avoid coughing)
9. Injection of Teflon or bovine collagen in the submucosal layer in the region of the bladder neck. This leads to narrowing of the urethral lumen and increased urethral resistance.

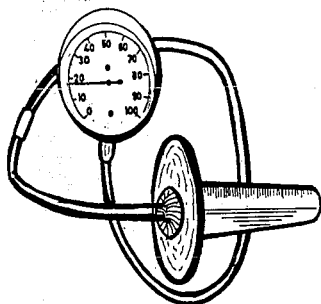


Fig.113. Kegel perineometer

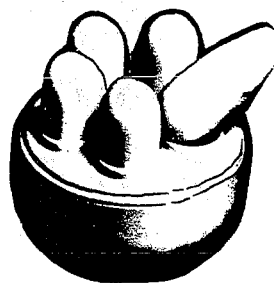


Fig.114. Vaginal cones

III. Surgical Treatment

It is the primary treatment of stress incontinence. The operation is done vaginally, abdominally, or abdominovaginally. Almost 200 operations have been described.

A. Vaginal Operations

1. Kelly operation. It consists of repair of cystocele and/or urethrocele. The paraurethral tissue on both sides is then brought to the midline using vertical interrupted mattress sutures. In this way we plicate the whole urethra and bladder neck. This gives support to the urethra and restores the normal posterior urethrovesical angle. Operation is done for mild and moderate cases of stress incontinence. Long term success rate is 55-65%.
2. El-Hemaly urethrorrhaphy operation. A vertical incision is made in the anterior vaginal wall. The torn edges of the internal urethral sphincter are sutured together to restore its integrity. The repair restores the normal urethrovesical angle seen in continent women.
3. Tension-free-vaginal tape (TVT) operation. The tape is made of prolene and has a curved needle at each end. Operation is done using local infiltration anaesthesia. Two small transverse incisions 5 cm apart are made in the suprapubic area. A vertical incision is made in the anterior vaginal wall. The needles of the tape are passed upward behind the pubic bone and brought out through the suprapubic incisions. The tape is made to surround the mid-urethra. The cystoscope is used by the assistant to make sure that the bladder is not pierced by the needle. The tape is adjusted by pulling on its ends, and continence is confirmed by asking the patient to cough. The ends of the tape are cut off and left free and not fixed to the tissues. Finally the vaginal and suprapubic incisions are closed. Operation takes 20-30 minutes. The cure rate is about 85%.
4. Transobturator tape (TOT) operation. A synthetic tape (prolene) is passed through the obturator foramen to support the mid-urethra. It avoids bladder perforation which may occur with TVT operation. In TOTO the tape is passed through the obturator foramen from inside out (O).

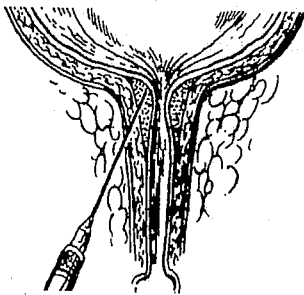


Fig. 114-2. Periurethral injection of bovine collagen



Fig. 114-3. Vaginal tape operation

B. Abdominal Operations

1. Mashall-Marchetti-Krantz. The stitches are placed in the fascia on each side of the bladder neck and upper half of the urethra and are attached to the periosteum on the back of the symphysis pubis. This restores the normal intra-abdominal position of the urethra. Main complication is osteitis pubis (0.5-5%). Nonabsorbable (as mersilene) or delayed absorbable sutures (as Vicryl or Dexon) are used.
2. Burch Operation. Burch colposuspension is the operation of choice. It corrects both stress incontinence and cystocele. The stitches are placed in the fascia on each side of the bladder neck and the base of the bladder and are attached to the iliopectineal ligaments (Cooper Ligaments). Nonabsorbable or delayed absorbable sutures are used. Operation can be done through the laparoscope.

The success rate of the above abdominal operations is 80-90%.

C. Combined Abdominovaginal Operations

1. Sling Operations

Autogenous fascia (rectus sheath, fascia lata, round ligaments) or synthetic material (nylon, polyethylene) is placed below the bladder neck to form a sling. An example is Aldridge sling operation in which two strips from the anterior rectus sheath are brought down behind the symphysis pubis and stitched below the bladder neck.

2. Needle Bladder Neck Suspension Operations

An incision is made in the vaginal wall to expose the bladder neck. A nylon suture is placed in the fascia on each side of the bladder neck. The two sutures are passed upward behind the symphysis pubis using a special needle and are attached to the anterior rectus sheath. The cystoscope is used to be sure that the needle does not pass through the bladder (endoscopic needle bladder neck suspension). An example is Stamey operation in which two Dacron tubes (1 cm) are used to give support to the bladder neck and to avoid the sutures cutting through the tissues.

D. Artificial Urinary Sphincter

Indicated when surgery fails to correct stress incontinence. The device consists of a cuff which is placed around the bladder neck. A balloon reservoir, containing fluid is placed in the peritoneal cavity or under the anterior rectus sheath, and a small pump is situated in one labium major. Under normal conditions the cuff is full with fluid thus closing the bladder neck. When voiding is desired, the pump is pressed to force the fluid in the cuff to go back into the balloon reservoir so that voiding can occur. The cuff then gradually refills over the next few minutes.

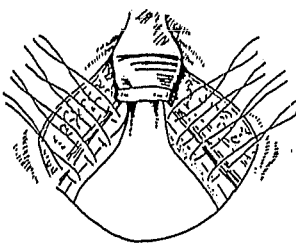


Fig.115. Burch operation

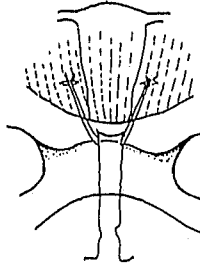


Fig.116. Stamey

operation

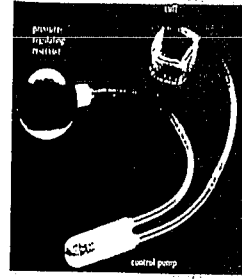


Fig.117. Artificial urinary sphincter

A New Concept in the Aetiology and Treatment of Urinary Incontinence

A new concept is put forward by Professor Abdel Karim El-Hemaly, explaining the mechanism of micturition and the factors responsible for urinary continence and causes of urinary incontinence and its treatment.

Urinary continence depends on two main factors, one inherent and one acquired.

- I. The acquired factor is an acquired behaviour gained by learning and training in early childhood how to maintain a high alpha-sympathetic tone at the internal urethral sphincter, keeping it closed all the time till there is a need or desire to void.
- II. The inherent factor is the presence of an intact and strong internal urethral sphincter. The latter is a collageno-muscular cylinder that extends from bladder neck down to the perineal membrane. It is lined by urothelium. The smooth muscle fibres lie on top and intermingle with the collagen fibres in the midthickness of the cylinder. The muscle fibres are connected above with the detrusor muscle and are controlled by alpha-sympathetic nerves T10-L2. These muscle fibres are responsible for the closure and opening of the internal urethral sphincter.

Functional errors or structural damage of the internal urethral sphincter will result in different types of voiding troubles, e.g., failure to gain the acquired behaviour of keeping a high alpha-sympathetic tone at the internal urethral sphincter will lead to nocturnal enuresis. Also structural damage of the internal urethral sphincter due to traumatic injury like childbirth trauma, degeneration caused by infection and/or atrophy due to oestrogen deficiency, will lead to detrusor overactivity (D.O.), stress urinary incontinence (S.U.I.) or mixed type of urinary incontinence depending on the level and extent of rupture in the internal urethral sphincter. Because of the intimate relation of the internal urethral sphincter to the anterior vaginal wall, overstretching of the vagina during childbirth will tear the sphincter. If the upper part is torn it will lead to D.O. If rupture affects the lower part, this will lead to S.U.I. If the whole length is torn this will lead to a mixed type of urinary incontinence. Understanding this mechanism, a new operation is innovated to treat such troubles, urethro-raphy (see before). Another

operation, urethroplasty is further introduced, where after mending the torn sphincter wall, a vaginal flap is put on the mended wall for further support, and as an autologous collagen source.

DETRUSOR OVERACTIVITY

The patient complains of urgency incontinence, frequency, and nocturia, and maybe incontinence at orgasm. Involuntary loss of urine also occurs when the woman sits for a long time and stands to go to the bathroom. She may pass urine with the sight or sound of water, so while washing dishes she develops a sudden urge to void and will urinate before reaching the bathroom. Cystometry confirms the diagnosis. Involuntary detrusor contractions of 15 cm of water or more occur during filling of the bladder.

AETIOLOGY. See page 331.

TREATMENT

1. Bladder drills. The patient is asked to pass urine every hour during daytime and to increase the interval by 15 minutes every week until she passes urine every 2-3 hours.
2. Drugs which inhibit the contractions of detrusor muscle as anticholinergic drugs, tricyclic antidepressants, and ephedrine.

Notes for the postgraduate

- Ephedrine stimulates alpha-adrenergic receptors in the internal urethral sphincter leading to contraction, and stimulates beta-adrenergic receptors in the detrusor muscle leading to relaxation.
- Three to 30% of women suffer from detrusor overactivity after surgical treatment of genuine stress incontinence. This is explained by (a) the original incontinence was due to detrusor overactivity; (b) the patient had both types of incontinence before surgery; (c) surgery created local lesions leading to detrusor overactivity, e.g. overcorrection of the support of the bladder neck leading to bladder outflow obstruction. This obstruction can cause detrusor overactivity. Also damage of the autonomic nerves in the pelvis during displacement of the bladder.
- About 35% of women with stress incontinence have also detrusor overactivity.

CHRONIC PELVIC PAIN

Chronic pelvic pain refers to pain lasting more than 6 months. It is one of the most common complaints in gynaecology.

AETIOLOGY

I. Gynaecological Causes

A. Cyclic Pain

1. Primary dysmenorrhoea.
2. Secondary dysmenorrhoea.
3. Adenomyosis.
4. Ovulation (Mittelschmerz) pain.
5. Haematocolpos as in case of imperforate hymen.
6. Pelvic congestion or pelvic pain syndrome (PPS).

B. Acyclic Pain

1. Chronic pelvic inflammatory disease.
2. Endometriosis.
3. Uterine prolapse.
4. Ovarian cysts, tumours and polycystic ovaries.
5. Uterine neoplasms; fibroids and malignant tumours.
6. Intrauterine contraceptive device.
7. Residual ovary syndrome.
8. Pelvic adhesions. Responsible for about 40% of the cases.
9. Universal joint syndrome. Laceration of uterosacral ligaments may occur at the time of a traumatic delivery allowing free rotation of the uterus like a universal joint. Lacerations are diagnosed by laparoscopy.

II. Nongynaecological Causes

Pain may be related to urinary tract, gastrointestinal tract, musculoskeletal system and some systemic diseases.

A. Urinary

Urethritis, cystitis, calculus, chronic urinary retention, and malignancy.

B. Small bowel

Chronic appendicitis and regional ileitis (Crohn's disease).

C. Large bowel

Ulcerative colitis, diverticulitis, irritable bowel syndrome, constipation, and tumours.

D. Musculoskeletal

These include diseases of muscle, ligaments, bone and joints as disc lesions, spinal osteoarthritis, and spondylolithesis.

E. Systemic Diseases

Pelvic pain may occur in systemic lupus erythematosus and Munchausen syndrome.

III. Psychogenic Pelvic Pain

It is not diagnosed until other causes of pain are excluded and the patient emotional status has been investigated.

IV. Idiopathic Pain

In some cases no cause is found to explain chronic pelvic pain.

DIAGNOSIS OF CHRONIC PELVIC PAIN

A. History

This includes:

1. Characteristics of pain
 - mode of onset; acute or chronic
 - site of pain
 - nature; colicky or aching
 - degree; mild or severe
 - duration
 - continuous or intermittent
 - localization; localized or radiating
 - relation to menses; cyclic or acyclic
 - associated symptoms.
2. Menstrual, obstetric, past and sexual history.
3. Gastrointestinal and urinary symptoms.

B. Physical Examination

It includes general, abdominal, pelvic and rectal examinations.

C. Investigations

These depend upon the history and physical examination.

1. Laboratory tests. Complete blood count, erythrocyte sedimentation rate (ESR) and urinalysis. ESR is nonspecific and is increased in any inflammatory condition.
2. Ultrasound. It detects pelvic masses and polycystic ovaries, pelvic veins diameters can be measured by colour Doppler ultrasound.
3. CT scan and MRI. Can detect pelvic masses and assess malignant lesions.
4. X-Ray examination:
 - a. Intravenous pyelogram if urinary symptoms are present.
 - b. Barium enema if bowel symptoms are present.
 - c. Plain X-ray of lumbosacral spine if there is clinical evidence of musculoskeletal disease.
 - d. Pelvic venography to diagnose pelvic congestion syndrome.

5. Laparoscopy. Indicated for patients with unexplained chronic pelvic pain. It may reveal small areas of endometriosis, pelvic adhesions, or dilated veins may be seen in the broad ligament and around the ovaries in PPS.

TREATMENT

1. Treatment of the cause.
2. Psychotherapy. For cases with psychogenic pain.

THE RESIDUAL OVARY SYNDROME

One or both normal ovaries may be left at hysterectomy to avoid menopausal symptoms. In some cases the patient complains of chronic lower abdominal pain, with or without dyspareunia. Pelvic examination reveals a unilateral tender pelvic mass, which at laparotomy, is found to contain a cystic ovary with surrounding adhesions.

THE PELVIC CONGESTION SYNDROME (PELVIC PAIN SYNDROME-PPS)

Clinical Picture

The syndrome occurs in the multiparous, emotionally unstable women. It is due to vascular congestion of the uterus and blood vessels of the broad ligament (pampiniform plexus of veins). There is a dull aching pain which increases premenstrually. It is felt in one iliac fossa more commonly on the right side, but it may move from side to side. It is increased by fatigue, walking, and standing and becomes less when lying flat. It is associated with deep dyspareunia and postcoital ache. Menorrhagia and urinary frequency may be present.

Deep pressure on the ovarian point which is at the junction of the upper and middle thirds of a line joining the umbilicus and anterior superior iliac spine causes pain in the iliac fossa on that side (site of the ovary). It is due to compression of the ovarian vein as it crosses the transverse process of the second and third lumbar vertebrae. The uterus is slightly enlarged, soft, and retroverted. Vaginal examination reveals a congested vagina with a blue or violet colour.

Aetiology

The true cause is unknown. The following lesions may be responsible.

1. Chronic parametritis.
2. Congested and sclerocystic ovaries.
3. Pelvic congestion. This is the most accepted explanation. In some patients, pelvic venogram shows dilated pelvic veins (pelvic varicosities). Dilatation of pelvic veins is attributed to:
 - a. Excessive oestrogen stimulation. Oestrogen causes dilatation of pelvic veins, or
 - b. Emotional stress which causes pelvic congestion due to disturbance of the pelvic autonomic nervous system, or
 - c. Anatomical factor as the pelvic veins are thin walled and devoid of valves, or

- d. The presence of unknown vasodilator substance.

However, most women with pelvic varicosities have no pain.

Investigation of PPS

1. Ultrasonography. The uterus is enlarged, the endometrium is thickened, and the ovaries are frequently cystic. Colour Doppler ultrasound may show dilated veins in the broad ligament and around the ovaries.
2. A pelvic venogram during an acute attack of pain may demonstrate pelvic varicosities. A special needle is passed through the cervix to reach the fundus, then 20 ml of Urografin is injected into the myometrium. The spread of the dye into the pelvic veins will be seen and assessed on the fluoroscopic screen.
3. Laparoscopy. Indicated for patients with unexplained chronic pelvic pain. The uterus appears dark blue and mottled. Dilated veins may be seen in the broad ligament and around the ovaries. However, not all women with such findings complain of pelvic pain.

Treatment of PPS

1. Medical Treatment

Inhibition of ovarian activity assuming that the syndrome is caused by excessive oestrogen. A large dose of a progestogen is given continuously for 6 months. This reduces the secretion of oestrogen, the diameter of pelvic veins, the size of the uterus and endometrial thickness, and relieves pain (Provera oral tablets 30 mg/day).

2. Surgical Treatment

Hysterectomy and bilateral salpingo-oophorectomy in old women who completed their families.

3. *Psychotherapy*. For cases with psychogenic pain.

LOW BACKACHE

AETIOLOGY

1. Gynaecological Causes

- Chronic cervicitis. Pain occurs if infection spreads along the uterosacral ligaments leading to sacralgia.
- Uterine prolapse and retroversion. Pain is due to pelvic congestion and stretching of the uterosacral ligaments.
- Pelvic congestion due to any cause (see congestive dysmenorrhoea).
- Tumours. With a large abdominal tumour the muscles of the back may become strained to maintain lordosis necessary for the patient's balance. A tumour impacted in the pelvis causes sacral ache. Infiltration of uterosacral ligaments by malignancy or endometriosis causes low backache.

2. Nongynaecological Causes

- Lesions of the urinary tract. Diseases of the kidney or ureter may cause backache.
- Lesions of the gastrointestinal tract. Lesion or carcinoma of the rectum can cause sacral pain.
- Musculoskeletal lesions. These include diseases of muscle, ligaments, bone and joints as rheumatic conditions and disc lesions.

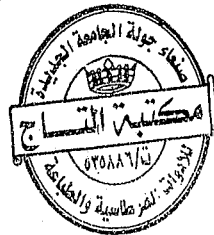
3. Psychogenic Pain

It is not diagnosed until other causes of pain are excluded and the patient's emotional status has been investigated.

4. Idiopathic Pain

In some cases no cause is found to explain low backache.

N.B.: Backache caused by a gynaecological lesion is diffuse, deep-seated and not accompanied by tenderness. Its level is sacral or lumbosacral and not felt higher than the fourth lumbar vertebra.



VAGINAL CYTOLOGY

Malignant cells may be exfoliated from a tumour in the vagina, cervix, endometrium, tube or even in the ovary. The aim of cytology is to screen symptom-free women for the diagnosis of early malignancy in the genital tract. However, the diagnosis should be confirmed by biopsy.

TECHNIQUES

1. The Cervical Smear

A cervical smear is recommended for routine examination of the genital tract (page 232). The method detects early cervical carcinoma in about 95% of cases, endometrial carcinoma in 50% of cases, tubal carcinoma in 20% and ovarian cancer in 10-20% of cases. The false negative results can be explained by (1) not all cancers exfoliate abnormal cells; (2) abnormal cells are exfoliated but not sampled by the doctor due to faulty technique; (3) there can be abnormal cells on the slide, but not detected by the screener; (4) too thick, too thin, presence of blood, or dried smear before fixation will not show abnormal cells. Infection due to human papillomavirus or *Trichomonas vaginalis* may lead to a false positive result. The smear taken directly from the cervix can diagnose dyskariosis, carcinoma in situ, microinvasive carcinoma and frankly invasive cancer. The cervical smear is done in all sexually active women, regardless of age and repeated until the patient is 60 years of age. The main aim is to detect early cervical carcinoma. In the USA, the smear is repeated every year in high risk patients and every three years in low risk patients. In the UK the figures are 3 and 5 years.

2. The Endometrial Smear

It detects endometrial carcinoma in up to 90% of cases. The specimen is obtained from the uterine cavity using a minute rotating brush or sterile saline is injected then aspirated using a special cannula e.g. Barbaro endometrial cannula. The material obtained is fixed and stained by Papanicolaou method. The endometrial smear, endometrial biopsy, or endometrial aspiration may be taken every 1-2 years from the postmenopausal patient who has a high risk factor. The risk factors include obesity, diabetes mellitus, delayed menopause (>52 years), family history of endometrial carcinoma, and women receiving tamoxifen therapy for breast carcinoma.

INDICATIONS OF VAGINAL SMEAR

A. Gynaecological Indications

1. Diagnosis of early malignancy in the genital tract.
2. To follow up the patient after treatment of the malignant lesion to detect early recurrence.
3. Detection of ovulation.
4. Diagnosis of vaginal infections as *trichomonas* and *candida*.

5. Detection of chromatin (Barr) body for nuclear sexing, however, the buccal smear is preferable.

Obstetrical Indications

Premature rupture of membranes. The amniotic fluid shows positive fern test.

THE DIFFERENT METHODS OF CYTODIAGNOSIS

1. Cervical smear.
2. Endometrial smear.
3. Vaginal smear. For follow up after hysterectomy for malignant lesions.
4. Breast smear.
5. Buccal smear for nuclear sexing.
6. Cytologic examination of pleural effusion, ascitic fluid or peritoneal washings for malignant cells.

DIFFERENTIAL DIAGNOSIS IN GYNAECOLOGY

PELVI-ABDOMINAL MASS

AETIOLOGY

1. Uterine Causes

A. Normal Pregnancy

Pregnancy is the commonest cause of an abdominal swelling in the childbearing period, and should be excluded before any diagnosis is made. The patient is in the childbearing period with symptoms and signs of pregnancy in the form of amenorrhoea, quickening and breast signs of pregnancy, etc. The uterus is felt as a soft or cystic swelling with a convex upper border. Intermittent contractions may be detected on palpating the mass (Braxton Hicks contractions). A uterine souffle may be heard. The palpation of fetal parts, auscultation of fetal heart sounds and umbilical souffle are sure signs of pregnancy. A pregnancy test or sonar confirms the diagnosis in case of doubt.

b. Abnormal Pregnancy

This may be in the form of hydatidiform mole, polyhydramnios, and advanced extrauterine pregnancy.

c. Fibroids

The patient is usually above 35 years and nullipara.

Symptoms

Menorrhagia is the commonest symptom.

Signs

Typically the swelling is irregular or knobby due to the presence of multiple fibroids. It is firm in consistency, mobile, not tender and dull on percussion. A uterine souffle may be heard due to increased vascularity. Vaginally, the swelling is continuous with the uterus and moves with movement of the cervix. If a uterine sound is introduced it will show enlargement of the uterine cavity in case of submucous and interstitial fibroids.

d. Large Haematometra

It is due to cervical stenosis which may be congenital or acquired after cauterization or amputation of the cervix. There is amenorrhoea and abdominal pain recurring every month. The uterus is symmetrically enlarged and the uterine sound can't be passed through the stenosed cervix.

e. Large Pyometra

The clinical features are mentioned on page 136.

2. Tubal Causes

In rare cases a hydrosalpinx or pyosalpinx is felt above the inguinal ligament. On bimanual examination, an elongated cystic mass is felt in the region of the adnexa. It is usually bilateral and tender. The uterus may be fixed in retroversion.

3. Ovarian Tumours

The patient is of any age and parity.

Symptoms

An abdominal swelling is the main complaint. Menstruation is not affected by benign or malignant tumours even bilateral, however, it is affected by functioning tumours. Pain is absent unless there is a complication as torsion or malignancy.

Signs

The swelling is smooth or irregular if multilocular. It is cystic with a fluid thrill. Solid areas may be felt in a cystic swelling, sometimes the whole tumour is solid. It is mobile unless fixed by adhesions, not tender unless there is a complication as infection or malignancy. The tumour is dull on percussion. The flanks are resonant unless there is associated ascites. Vaginally, the lower pole may be palpated and is felt separate from the uterus.

4. Parametric Causes

a. Acute Parametritis

See the clinical picture on page 143.

b. Broad Ligament Cyst

It is sometimes large enough to be felt abdominally. A cystic mass of limited mobility is felt to one side of the uterus and pushing it to the opposite side.

c. Broad Ligament Haematoma

Its causes are rupture of tubal pregnancy or varicose veins in the broad ligament, incomplete rupture of the uterus, and incomplete haemostasis after pelvic operation, especially after removal of a broad ligament tumour. A cystic mass of limited mobility is felt to one side of the uterus and pushing it to the opposite side. It is associated with signs of internal haemorrhage.

5. Mass In Douglas Pouch

a. Pelvic Haematocele

In the majority of cases, it is the result of ruptured tubal pregnancy, so there is a history suggestive of disturbed ectopic pregnancy in the form of recurrent attacks of lower abdominal pain, fainting and vaginal bleeding after a period of amenorrhoea. The collection of blood in Douglas pouch leads to pressure symptoms in the form of dysuria, dyschezia and dyspareunia.

There is a pelvi-abdominal mass which is fixed, tender and ill-defined. On percussion areas of resonance may be detected due to adherent intestine. Vaginally, there is a fixed, tender mass bulging through the posterior fornix. The uterus is pushed forwards. It is slightly enlarged and soft. Aspiration of Douglas pouch by a needle reveals blood and confirms the diagnosis.

b. Pelvic Abscess

Aetiology

It may follow salpingitis, appendicitis, diverticulitis, septic abortion, puerperal sepsis, infection of pelvic haematocoele, or surgery as hysterectomy.

Diagnosis

History of pelvic infection or surgery. There is fever, malaise, pelvic pain, dyspareunia, dysuria, dyschezia and mucus diarrhoea. Vaginally, a tender cystic mass is felt bulging through the posterior fornix. Aspiration of Douglas pouch reveals pus.

Treatment

Under general anaesthesia, the posterior vaginal fornix is incised and pus evacuated (posterior colpotomy), pus is sent for aerobic and anaerobic culture and sensitivity test. Sometimes, laparotomy is needed as in case of ruptured tubo-ovarian abscess. The low oxygen content in the closed cavity favours growth of anaerobic organisms.

6. Haematocolpos

It is due to imperforate hymen or transverse vaginal septum. The mass is cystic and has a limited mobility. The uterus may be felt as a small firm nodule on the top of the mass. Vaginal examination shows a blue, closed bulging hymen. Rectal examination shows a cystic mass anterior to the rectum and continuous with the abdominal swelling.

7. Extragenital Swellings

a. Distended Bladder

Pressure on the mass initiates the desire to micturate. The mass disappears after micturition or catheterization of the bladder.

b. Large Hydronephrosis

A renal swelling is oval in shape and can be pushed into the loin. There is a band of resonance over the tumour caused by the colon. Intravenous pyelography confirms the diagnosis.

c. Encysted Tuberculous Peritonitis

It resembles an ovarian cyst. It is characterized by: (1) history of tuberculosis; (2) symptoms and signs of tuberculous toxæmia as loss of appetite and weight; (3) amenorrhoea is common; (4) the swelling is tender, fixed, ill-defined with areas resonant

(intestine) and areas dull (fluid); (5) the blood picture shows anaemia, lymphocytosis and high sedimentation rate; (6) tuberculin test, if negative it excludes tuberculosis; (7) plain X-ray to the chest and abdomen. The latter may show calcified mesenteric glands.

d. Retroperitoneal Tumour

As fibroma or sarcoma. The swelling is fixed and resonant on percussion due to overlying intestine.

e. Pancreatic and Mesenteric Cyst

The swelling cannot be pushed into the pelvis. There are areas of resonance over the mass due to adherent intestine.

f. Faecal Mass

Due to loaded caecum or sigmoid colon. It is felt as a soft mobile, tubular mass. If suspected, reexamination is done after cleansing enemas.

8. Other Causes which Lead to Abdominal Enlargement

As ascites, flatulence, false pregnancy and obesity.

9. Tumours of the Abdominal Wall

These become more prominent and more easily palpable when the rectus abdominis muscle contracts by asking the patient to lift the shoulders from bed while the arms are folded on the chest.

MASS IN DOUGLAS POUCH

1. Uterine

- a. Retroverted uterus. It is the commonest mass felt through the posterior vaginal fornix.
- b. Posterior wall fibroid.

2. Tubal

- a. Hydrosalpinx or pyosalpinx.
- b. Tubal pregnancy.
- c. Tubal neoplasm.

3. Ovarian

- a. Ovarian mass.
- b. Prolapsed ovary.

4. Mass in Douglas pouch itself

- a. Pelvic haematocoele.
- b. Pelvic abscess.
- c. Endometriosis of pelvic peritoneum.
- d. Encysted tuberculous mass.

- e. Metastatic nodules, specially from cancer of ovary.
 - f. Inflammatory mass as appendicular mass or bilharzial mass of the colon.
5. **Pelvic kidney**
6. **Retroperitoneal Tumour**
As fibroma, sarcoma and tumours of the sacrum as osteoma.
7. **Mass in the Rectum**
(a) Faecal mass; (b) cancer of rectum; (c) endometriosis of the rectovaginal septum and (d) foreign body.

VAGINAL CYSTS

1. Gartner cyst which is the commonest (page 107).
2. Hymeneal cyst which arises from the lower part of the Wolffian (Gartner) duct.
3. Müllerian cysts. Small cysts, single or multiple and lined by epithelium similar to that lining the cervical canal and contain mucus. They are thought to arise from displaced cervical glands.
4. Cyst of the Skene tubules.
5. Implantation dermoid (page 217).
6. Endometriotic cysts. These can arise in scars in the vagina due to implantation of endometrial fragments following childbirth or uterine curettage. However, they are mostly seen in the posterior fornix in association with endometriosis of the rectovaginal septum.
7. Vaginitis emphysematosa (page 129).

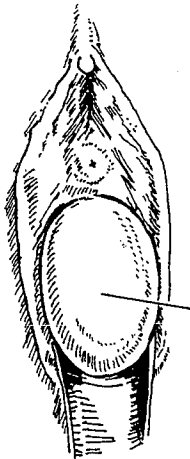


Fig.118. Gartner cyst



Fig.119. Cyst of Skene tubule

MASS PROTRUDING FROM THE CERVIX

1. Cervical polyp of any type (page 247).
2. A polyp arising from the body of uterus may protrude through the cervix. The uterine sound shows that the pedicle is not attached to the cervix.
3. The inverted uterus.
4. Inevitable and incomplete abortion.

CAUSES OF CERVICAL ENLARGEMENT

(1) Congenital hypertrophy; (2) congestion and oedema due to pregnancy, uterine prolapse and cervicitis; (3) granulomatous lesions as syphilis, bilharziasis, tuberculosis, and amoebiasis; (4) cervical pregnancy; (5) cervical endometriosis; (6) benign and malignant neoplasms.

CONTACT BLEEDING

It is bleeding occurring after intercourse, vaginal examination or douching.

Aetiology. (1) Carcinoma of the cervix; (2) ulcers of the cervix; (3) vascular erosion; (4) cervical polypi; (5) vaginal carcinoma; (6) granulation tissue in the vaginal vault after total hysterectomy.

Management. The case should be investigated by cervical smear or colposcopy to exclude malignancy. The treatment is directed to the cause.

CAUSES OF SYMMETRICAL ENLARGEMENT OF THE UTERUS

(1) Pregnancy; (2) ectopic pregnancy; (3) subinvolution of the uterus; (4) metropathia haemorrhagia; (5) submucous or single interstitial fibroid; (6) diffuse adenomyosis; (7) haematometra (8) pyometra; (9) early malignant tumour as carcinoma, sarcoma or choriocarcinoma.

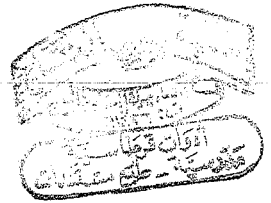
CAUSES OF UTERINE CASTS

1. Membranous cast in membranous dysmenorrhoea.
2. Blood cast made of coagulated blood in case of menorrhagia.
3. Decidual cast. This may be passed in abortion and ectopic pregnancy. It consists of decidual cells and chorionic villi in case of abortion, but no chorionic villi are present in ectopic pregnancy.

4. Malignant cast. Occasionally, the patient with endometrial carcinoma or sarcoma passes a piece of polypoid growth per vagina.

CAUSES OF TUBAL SWELLING

- | | |
|----------------------|---------------------|
| (1) Hydrosalpinx. | (2) Pyosalpinx, |
| (3) Tubal pregnancy, | (4) Tubal neoplasm. |



CAUSES OF HAEMATOSALPINX

(1) Torsion of a hydrosalpinx; (2) torsion of the normal fallopian tube which is very rare; (3) tubal pregnancy; (4) endometriosis of the tube; (5) malignant tumour; (6) gynaetresia due to imperforate hymen, transverse vaginal septum and cervical stenosis. The latter may be congenital or acquired after cauterization or amputation of the cervix.

ADNEXAL MASS

Anatomically, the adnexa consist of the fallopian tubes, ovaries, round ligaments and broad ligaments. The adnexal swelling may arise from:

1. **Ovary.** Functional cyst, cystic neoplasm, solid neoplasm, ovarian endometriosis and ovarian pregnancy.
2. **Tube.** Hydrosalpinx, pyosalpinx, tubal pregnancy and neoplasm.
3. **Broad ligament.** Paraovarian cyst and broad ligament fibroid.
4. **Uterus.** Pregnancy in a bicornuate uterus and pedunculated subserous fibroid.
5. **Bowel.** Appendicitis, diverticulitis and colonic cancer. Caecum or sigmoid distended with gas or faeces.
6. **Miscellaneous.** Distended bladder which may be mistaken for an ovarian cyst, urachus cyst, pelvic kidney and retroperitoneal neoplasm.

GYNAECOLOGICAL CAUSES OF ACUTE ABDOMINAL PAIN

1. Ovarian causes. Complication in an ovarian cyst as torsion, haemorrhage and rupture. Rupture of chocolate cyst. Haemorrhage into a graafian follicle or corpus luteum. Ovulation pain.
2. Tubal causes. Acute salpingo-oophoritis, ruptured ectopic pregnancy, torsion of a hydrosalpinx, and torsion of normal adnexa (very rare).
3. Complication in a fibroid. Red degeneration, torsion of a pedunculated subserous fibroid, and rupture of a vein on the surface of a subserous tumour.
4. Pelvic peritonitis due to any cause and ruptured tubo-ovarian abscess.
5. Perforation of the uterus during insertion of an intrauterine contraceptive device.
6. Retrograde menstruation. Blood causes irritation of pelvic peritoneum and pain.

CAUSES OF A SHORT PERIOD OF AMENORRHOEA FOLLOWED BY BLEEDING

(1) Abortion; (2) hydatidiform mole; (3) ectopic pregnancy; (4) metropathia haemorrhagica; (5) persistent corpus luteum, bleeding occurs when it degenerates.

CAUSES OF HAEMORRHAGE IN THE OVARY

(1) Ovarian endometriosis; (2) ovarian pregnancy (3) malignant tumour; (4) haemorrhage in an ovarian cyst, e.g. after torsion; (5) haemorrhage into a graafian follicle or corpus luteum; (6) overstimulation of the ovaries by Clomid or gonadotrophins.

CAUSES OF PELVI-ABDOMINAL SWELLING ASSOCIATED WITH IRREGULAR VAGINAL BLEEDING

(1) Abortion; (2) hydatidiform mole; (3) ectopic pregnancy (4) fibroids; (5) malignant tumour of the body of the uterus; (6) functioning and malignant ovarian tumours.

CAUSES OF ABDOMINAL PAIN ASSOCIATED WITH IRREGULAR VAGINAL BLEEDING

(1) Abortion; (2) hydatidiform mole; (3) ectopic pregnancy; (4) haemorrhage into or rupture of a corpus luteum; (5) fibroid polyp; (6) malignant tumour of the genital tract; (7) ovulation pain and ovulation bleeding; (8) after insertion of intrauterine contraceptive device.

CAUSES OF PELVI-ABDOMINAL SWELLING ASSOCIATED WITH AMENORRHOEA

(1) Pregnancy; (2) false pregnancy (pseudocyesis); (3) androgenic ovarian tumours; (4) encysted tuberculous peritonitis; (5) haematocolpos and haematometra due to imperforate hymen, transverse vaginal septum or cervical stenosis.

HORMONE AND ANTIHORMONE THERAPY IN GYNAECOLOGY

HORMONES

1. Oestrogens.
2. Progestogens.
3. Combined contraceptive tablets.
4. Human pituitary gonadotrophins.
5. Human menopausal gonadotrophins.
6. Purified urinary follicle stimulating hormone (FSH).
7. Highly purified urinary FSH.
8. Recombinant FSH.
9. Human chorionic gonadotrophin (HCG).
10. Recombinant HCG.
11. Recombinant LH.
12. Gonadotrophin releasing hormone.
13. Gonadotrophin releasing hormone analogues or agonists.
14. Gonadotrophin releasing hormone antagonists.

ANTIHORMONES

1. Antioestrogens:
 - a. Clomiphene citrate (Clomid).
 - b. Tamoxifen (Nolvadex).
 - c. Cyclofenil (Ondogyne).
2. Antiprogestogens:
 - a. Mifepristone.
 - b. Gestrinone.
3. Antiandrogens:
 - a. Cyproterone acetate.
 - b. Spironolactone.
 - c. Flutamide.
 - d. Finasteride.
4. Danazol.
5. Antigonadotrophins which are the gonadotrophin releasing hormone agonists and antagonists.
6. Dopamine agonists. They inhibit prolactin secretion. See hyperprolactinaemia.

OESTROGENS

A. Oestrogens produced in the human female

More than 20 oestrogens have been detected in the urine of the pregnant woman. However, only 3 are of clinical importance:

1. Oestrone (E1).
2. Oestradiol (E2). The major oestrogen secreted by the ovary. Some oestrone is also secreted by the ovary.
3. Oestriol (E3). It is the metabolite of oestrone and oestradiol and not secreted by the ovary.

B. Natural oestrogens

1. Conjugated equine oestrogens (Primarin).
2. Oestradiol 17-beta.
3. Oestradiol valerate.
4. Oestriol (Ovestin).
5. Piperazine oestrone sulphate.

C. Synthetic oestrogens

1. Ethinyl oestradiol.
2. Mestranol which is ethinyl oestradiol 3-methyl ether.

INDICATIONS OF OESTROGEN THERAPY

A. Gynaecological Indications

1. Disorders of menstruation:
 - a. Amenorrhoea and oligomenorrhoea.
 - b. Spasmodic dysmenorrhoea. The combined contraceptive tablet is used to inhibit ovulation.
 - c. Dysfunctional uterine bleeding.
 - d. Postponement or advancement of a menstrual period for religious or social reasons. The combined pill is used.
2. Cases of infertility due to scanty thick cervical mucus interfering with ascent of spermatozoa.
3. Diseases of vulva and vagina:
 - a. Vulvovaginitis of children.
 - b. Senile vaginitis.
 - c. Menopausal pruritus vulvae.
 - d. Trophic ulcers in case of prolapse.
 - e. Before and after vaginal operations in postmenopausal patients to help healing of tissues.

4. Menopausal syndrome. See the treatment of menopausal syndrome and the indications for hormone replacement therapy.
5. Contraception. For this indication oestrogen is combined with a progestogen. The morning-after pill may be used as a postcoital contraception (see hormonal contraceptives).
6. Endometriosis. Used as a combined contraceptive tablet.

B. Other Indications

1. Underdevelopment of the breasts.
2. Skin diseases as acne vulgaris and alopecia.
3. Atrophic rhinitis.
4. Carcinoma of prostate.

METHODS OF ADMINISTRATION

1. Oral. Examples of oral oestrogens are, ethinyl oestradiol (10 or 50 micrograms) and conjugated oestrogens (Primarin 0.625 and 1.25 mg).
2. Intramuscular. Oily solutions of oestradiol benzoate and propionate.
3. Subcutaneous. Capsules containing 25, 50 and 100 milligrams of oestradiol 17-beta are available. A capsule usually 50 mg is inserted subcutaneously in the abdominal wall once every 6 months (4-8 months) for menopausal syndrome.
4. Transdermal patch (Estraderm). Applied to the buttock twice weekly as action lasts 3-4 days. The patch gives 25, 50, 100 micrograms oestradiol 17-beta in 24 hours. For menopausal syndrome.
5. Vaginal cream, tablet and ring (Estring), for dry vagina and senile vaginitis.
6. Skin gel. Oestradiol 17-beta gel is applied to skin of legs or arms for menopausal syndrome. The dose is 1-5 mg daily.
7. Oestradiol nasal spray. Used to control hot flushes to avoid the large doses of oestrogen given orally. The dose is 100, 200, 300, or 400 micrograms daily.

PROGESTOGENS

A progestogen (progestin) is any substance which produces secretory changes in the endometrium which has been primed by oestrogen. Progesterone is the natural progestogen. Synthetic progestogens include derivatives of testosterone, 19-nortestosterone (19-norsteroids), 17-alpha-hydroxyprogesterone and other derivatives as gestodene.

INDICATIONS OF PROGESTOGEN THERAPY

A. Gynaecological Indications

1. Disorders of menstruation:
 - a. Amenorrhoea and oligomenorrhoea.

- b. Spasmodic dysmenorrhoea. The combined contraceptive tablet or dydrogesterone tablet (Duphaston) is used.
- c. Dysfunctional uterine bleeding.
- d. Postponement or advancement of a menstrual period.
- e. Premenstrual syndrome.
2. Cases of infertility due to luteal phase defect.
3. Menopausal syndrome. Given with oestrogen or alone if oestrogen is contraindicated as in liver disease.
4. Contraception. Used in the form of a combined pill with oestrogen, as progestogen-only pill (mini-pill) or injectable contraceptive (Depo-Provera) or hormone releasing intrauterine device or vaginal ring or subdermal contraceptive implants.
5. Endometriosis. Used as a combined contraceptive tablet or alone to produce a pseudopregnancy state.
6. Endometrial carcinoma. For advanced and recurrent cases as a palliative treatment.

B. Obstetrical Indications

Recurrent abortion due to luteal phase defect or given empirically.

METHODS OF ADMINISTRATION

1. Oral. Micronised progesterone (Utrogestan capsules) is given orally. Synthetic progestogens are given orally.
2. Intramuscular. Progesterone and other progestogens as 17-alpha-hydroxyprogesterone caproate (Primolut Depot and Proluton Depot) and medroxyprogesterone acetate (Depo-Provera) are given IM.
3. Progesterone suppositories inserted in the vagina or rectum.
4. Progesterone and levonorgestrel releasing intrauterine device.

COMBINED CONTRACEPTIVE TABLETS

INDICATIONS

1. Contraception.
2. Spasmodic dysmenorrhoea because anovulatory cycles are painless.
3. Treatment of ovulation pain.
4. Treatment of dysfunctional uterine bleeding.
5. Treatment of endometriosis by inducing a pseudopregnancy state for 9 months (6-12 months).
6. Treatment of premenstrual syndrome.
7. To postpone or advance menstruation for social or religious reasons.

HUMAN MENOPAUSAL GONADOTROPHINS (HMG)

HMG are obtained from the urine of postmenopausal women which contains large amounts of FSH and LH. The commercial preparation "Pergonal" or "Humegon" contains 75 or 150 IU of FSH and 75 or 150 IU of LH per ampoule. The preparation is contaminated with urinary proteins and so it must be given intramuscularly. If given subcutaneously it causes allergic reaction.

INDICATIONS

1. Hypothalamic-pituitary failure (WHO group I). There is anovulation and the gonadotrophin level is low.
2. Hypothalamic-pituitary dysfunction (WHO group 2). There is anovulation with a normal gonadotrophin level.
3. When clomiphene (Clomid) fails to induce ovulation.
4. Luteal phase defect.
5. Hostile cervical mucus. HMG improves the quantity and quality of cervical mucus.
6. Unexplained infertility.
7. To induce superovulation for intrauterine insemination and assisted reproductive techniques, as In Vitro Fertilization and GIFT procedure.
8. In the male to treat oligospermia and cryptorchidism.

METHOD OF ADMINISTRATION

- Treatment starts on the second or the third day of the cycle (spontaneous or induced) or at any time if the patient is amenorrhoeic.
- We usually start with 1 or 2 ampoules IM daily.
- On the 6th day of treatment we start monitoring the growth of follicles in the ovaries by repeated ultrasound and estimation of serum oestradiol. The dose is adjusted according to the ovarian response.
- When the leading graafian follicle is mature and ready to ovulate (diameter ≥ 18 mm and serum oestradiol is 1000-1500 picograms/ml) we inject 5000-10000 IU of human chorionic gonadotrophin (HCG) IM to induce ovulation.
- The patient is advised to have intercourse on the same day of HCG injection and again after 24 and 42 hours from that intercourse.
- If the level of serum oestradiol is above 2500 pg/ml, HCG is not injected to avoid ovarian hyperstimulation syndrome.
- Ovulation occurs in more than 90% per treatment cycle.
- Treatment is continued for 3-4 successive cycles.

SIDE EFFECTS

1. Multiple pregnancy. Twin pregnancy occurs in about 25% of cases. Triplets or more in about 5%.
2. Ovarian hyperstimulation syndrome occurs in 1-6% of cases (severe form 1%).
3. Increased incidence of abortion and preterm labour (10-30%) due to multiple pregnancy.
4. Increased incidence of ectopic pregnancy which occurs in about 3%, and heterotopic pregnancy in about 1%.

Notes

- HCG causes ovulation about 36 hours after its injection (the same with L.H peak).
- Picogram (pg) is micromicrogram, i.e. one trillionth of a gram.

HIGHLY PURIFIED HMG

Merional is given IM but also SC as it is highly purified, and so does not cause local allergic reaction which is caused by urinary proteins, and so can be given SC by the patient herself.

OVARIAN HYPERSTIMULATION SYNDROME (OHSS)

The syndrome is rare with Clomid but more frequent with gonadotrophins. It occurs only after injection of HCG, usually 3-6 days after the injection. Both ovaries are enlarged with multiple follicular cysts, many corpora lutea, and stromal oedema. The syndrome is temporary and usually disappears after one week. However, if the woman is pregnant, the syndrome will last for a longer time up to one month due to the presence of HCG which is secreted by the trophoblast and is responsible for the syndrome.

Pathogenesis

The syndrome is due to increased capillary permeability leading to shift of fluid from the intravascular to the extravascular space. This leads to hypovolaemia, hypotension, oliguria, haemoconcentration and venous thrombosis with embolism. As the renal perfusion is decreased, there is water and salt retention, oedema, increased weight, hyperkalaemia and acidosis with increased blood urea nitrogen (BUN) and serum creatinine.

Aetiology

The cause of increased capillary permeability, is not known. However, it is caused by the injection of HCG which may act by one of the following mechanisms:

- (1) Increased production of oestradiol by the ovaries; (2) release of a vasoactive substance from the ovaries; (3) release of histamine; (4) production of prostaglandins; (5) release of vascular endothelial growth factor from the luteinized granulosa cells; (6) release of cytokines; (7) release of interleukins 2, 6, and 8; (8) increased production of angiotensin II.

Clinical Picture

1. Mild form. There is ovarian enlargement without cyst formation, abdominal discomfort and weight gain.
2. Moderate form. There is ovarian enlargement with formation of ovarian cysts which are not large (5-12 cm in diameter), abdominal pain, nausea, vomiting and/or diarrhoea and weight gain.
3. Severe form. Large ovarian cysts are present with abdominal pain and distension, nausea, vomiting, and/or diarrhoea, ascites and may be pleural effusion and weight gain. There is hypovolaemia, hypotension, oliguria, and electrolyte disturbances. Thromboembolism may occur due to haemoconcentration.

Complications

1. Venous thrombosis and pulmonary embolism. It is due to haemoconcentration, high serum level of oestradiol, enlarged ovaries pressing on pelvic veins, and immobilization due to pain.
2. The enlarged ovaries may undergo torsion, or rupture with intraperitoneal haemorrhage.
3. Renal failure because of hypovolaemia, and reduced renal perfusion.
4. Liver dysfunction, and cholestatic jaundice caused by high serum oestradiol levels.
5. Respiratory distress and dyspnoea due to enlarged ovaries, ascites, and pleural effusion.
6. Adult respiratory distress syndrome as the increased capillary permeability leads to pulmonary oedema.

Prevention

1. Careful monitoring of the patient when the ovaries are stimulated with gonadotrophins. This is carried out by repeated ultrasound, and measurement of oestradiol levels. Cases with polycystic ovary syndrome (PCOS) are more liable to develop OHSS, and need special care.
2. Coasting. When serum oestradiol and number of ovarian follicles reach a critical level, which is determined by each center, we stop stimulation with gonadotrophins, and wait for several days till serum oestradiol, and number of follicles reach a safe level, then we administer HCG. The period of coasting is about 4-8 days. In general HCG is not administered if serum oestradiol is above 2500 picograms/ml.
3. Reduce the dose of HCG in the high risk patient, e.g. PCOS.
4. When luteal support is needed, use progesterone or dydrogesterone (Duphaston) and avoid HCG which is responsible for the syndrome.
5. Albumin is infused at the time of egg collection in the high risk patient (controversial). It increases the plasma oncotic pressure and keeps fluid in the intravascular space. It also combines with the vasoactive substances preventing their action on capillary permeability. Starch solution can be used instead of albumin, as it has a larger molecular weight, and will not pass easily into the extravascular space.

6. To avoid stimulation of the ovaries with gonadotrophins, immature oocytes are collected from the unstimulated ovaries early in the follicular phase. They are cultured for several days, and then fertilized before embryo transfer.
7. Cryopreservation of embryos to be used in a subsequent non-stimulated cycle.

Treatment

1. Mild form. No treatment, only rest at home and frequent follow-up.
2. Moderate and severe forms. Patient is admitted to hospital, and the following is done:
 - Complete rest in bed.
 - Avoid abdominal and vaginal examinations which may cause ovarian rupture.
 - Ultrasound to assess the size of the ovaries.
 - Analgesics for pain, e.g. Indocid 100 mg suppository twice daily.
 - Intravenous fluids to correct hypovolaemia, haemoconcentration and reduced renal perfusion. About 4 litres of Ringer lactate, or 5% glucose solution are given daily. The central venous pressure must be recorded.
 - Salt restriction to reduce ascites, and pleural effusion. Diuretics are contraindicated as they lead to hypovolaemia, shock, haemoconcentration and thrombosis.
 - Fluid chart to monitor fluid intake, and output.
 - Frequent recording of vital signs (pulse, temperature, blood pressure, and respiratory rate).
 - Daily recording of body weight.
 - Daily measurement of abdominal girth to detect increasing ascites.
 - Electrocardiogram may be needed to follow and evaluate hyperkalaemia.
 - Repeated estimation of haematocrit, plasma proteins, albumin-globulin ratio, BUN, serum creatinine, electrolytes, and liver function tests.
 - Coagulation profile.
 - Heparin is given in a prophylactic dose in cases with severe haemoconcentration (haematocrit >55 or white blood cells >25,000). However heparin may increase bleeding into the ovarian cysts.
 - Drainage of ascitic fluid (paracentesis) under ultrasound guide is needed in severe cases to relieve abdominal pain and respiratory distress. It is carried out abdominally or vaginally through Douglas pouch. As much fluid as possible is removed. Repeated drainage may be needed.
 - Laparotomy is only indicated if complication occurs in the enlarged ovaries in the form of torsion or rupture. The ovaries should be preserved – if possible – as they will return to their original size after disappearance of the syndrome.

PURIFIED URINARY FOLLICLE STIMULATING HORMONE

Metrodin is a pure urinary FSH. The ampoule contains 75 IU FSH and less than one unit LH. It is used to induce ovulation in case of polycystic ovary syndrome where the LH is already high. It is used in combination with HCG. The ovarian response is assessed as in case of HMG. The dose is 1-2 ampoules IM daily. The incidence of multiple pregnancy and abortions is less compared with HMG.

HIGHLY PURIFIED URINARY FSH

Metrodin high purity and Fostimon are HP-FSH. The drug is given IM or SC as it does not cause local allergic reaction, which is caused by urinary proteins, and so it can be given by the patient herself as it can be given SC.

RECOMBINANT FSH (PUREGON AND GONAL-F)

It is synthesized through genetic engineering. It is produced in the cells of the ovary of the Chinese hamster. The ovaries are transfected with the two subunit genes for FSH. It is given IM or SC. It has the following advantages over urinary FSH: (1) excellent results in ovulation induction; (2) more oocytes are retrieved for IVF; (3) high quality embryos and so higher pregnancy rate; (4) shorter treatment time; (5) more effective and so lower doses are given. The treatment is costly compared with urinary FSH or HMG.

HUMAN CHORIONIC GONADOTROPHIN (HCG)

HCG (Pregnyl, Profasi) is obtained from the urine of pregnant women and human placental tissue. Its action is similar to LH. It is given IM to stimulate the midcycle LH surge.

HIGHLY PURIFIED HCG

Choriomon is HP-HCG, and so can be given IM or SC.

RECOMBINANT HCG (OVIDREL)

It is synthesized through genetic engineering and is given SC.

RECOMBINANT LH

It is given SC. The recombinant HCG and LH may reduce the risk of ovarian hyperstimulation syndrome.

GONADOTROPHIN RELEASING HORMONE

GnRH (also called luteinizing hormone releasing hormone - LHRH - as it produces more LH than FSH), is secreted by the hypothalamus in pulses every 60-90 minutes in the follicular phase and every 120-180 minutes in the luteal phase. Synthetic GnRH is injected intravenously or subcutaneously every 60-90 minutes using a computerized pump to stimulate ovulation in clomiphene-resistant cases. The dose is 5 micrograms IV or 10 micrograms SC per pulse every 60-90 minutes. If the patient fails to respond, the dose is increased gradually by 5 micrograms each time. It is given for 2-4 weeks. Ovarian response is monitored by ultrasound. Ovulation occurs spontaneously by the endogenous LH surge. It does not cause ovarian hyperstimulation or multiple pregnancy which are hazards of HMG-HCG treatment.

Note. GnRH stimulates the pituitary to secrete FSH and LH because it is secreted in pulses. When it is given continuously not in pulses-it inhibits the secretion of these hormones, a condition called down regulation of the pituitary.

GONADOTROPHIN RELEASING HORMONE ANALOGUES (GnRH OR LHRH ANALOGUES OR AGONISTS)

These are synthetic compounds having the same action of GnRH. At first they increase the production of FSH and LH (stimulatory or flare-up effect). However, after 1-3 weeks, the secretion of FSH and LH is inhibited. This is known as pituitary down-regulation, and is due to the continuous, instead of the pulsatile use of the agonist.

INDICATIONS OF GNRH ANALOGUES

1. Treatment of idiopathic precocious puberty (inhibition of FSH, LH secretion).
2. Fibroids. The analogue is given for 3 months before myomectomy as maximum shrinkage occurs by the third month. It reduces vascularity and reduces the size of the myoma by 25-50%, so myomectomy becomes easier and with less blood loss. The effect of the drug is temporary as the myoma returns to its original size within 6 months after stopping treatment. The disadvantages are (a) in about 10% of cases, the tumour will not diminish in size due to lack of oestrogen receptors; (b) fibroids become small and may be missed at operation with subsequent high recurrence rate; (c) dense fibrosis may occur around the fibroid, and so removal becomes difficult.
3. Endometriosis. Given for 3 months before operation to make it easier and for 3-6 months after conservative surgery to inactivate residual lesions and reduce the frequency of recurrence. The analogue can be used as a primary treatment by inducing pseudomenopause for 6 months.
4. Dysfunctional uterine bleeding.
5. Idiopathic hirsutism. The drug inhibits the production of both oestrogens and androgens from the ovary.

6. Premenstrual syndrome.
7. For in vitro fertilization. To inhibit ovarian function before stimulation with HMG. This regimen prevents premature ovulation and cancellation of the treatment cycle as no ova can be retrieved, it also increases the number of ova retrieved, improves the quality of ova and reduces the risk of premature luteinization of follicles.
8. Prostatic carcinoma.

MODE OF ADMINISTRATION

1. Nasal Spray: As nafarelin (Synarel) and buserelin (Suprefact). For endometriosis the dose of nafarelin is 200 micrograms twice daily, and buserelin 300 micrograms three times daily.
2. Subcutaneous injection. Goserelin (Zoladex), 3.6 mg injected subcutaneously into the anterior abdominal wall. First injection is given during the first 5 days of the cycle and repeated every 4 weeks (28 days).
3. Intramuscular. Triptorelin (Decapeptyl), 3.75 mg injected during the first 5 days of the cycle and repeated every 4 weeks.

SIDE EFFECTS

1. Symptoms due to oestrogen deficiency in the form of hot flushes, headaches, reduced breast size, dry vagina, dyspareunia, decreased libido, and osteoporosis. Osteoporosis occurs if the analogue is given for more than 6 months.
2. Local irritation, erythema, and induration at the site of injection.
3. Anaphylactic reaction may occur.

ADD-BACK THERAPY

Osteoporosis occurs if the GnRH analogue (agonist) is given for more than 6 months. So to prevent osteoporosis, add-back therapy is started if the agonist is given for more than 6 months. We can give one tablet of tibolone (Livial) daily or an oestrogen-progestogen tablet similar to that used for postmenopausal hormone replacement therapy, e.g. conjugated oestrogens (Premarin), one tablet 0.625 plus oral medroxyprogesterone acetate (Provera) 2.5 mg daily.

GONADOTROPHIN RELEASING HORMONE ANTAGONISTS

The antagonists lead to immediate inhibition of the secretion of FSH, and LH without initial flare-up effect. They produce allergic side effects and local release of histamine. Like the analogues (agonists), they are used with HMG and urinary FSH to down-regulate the pituitary gland. Citrelix (Citrotide), and Ganirelix (Orgalutan) are used. The drug is injected subcutaneously into the lower abdominal wall. In the multiple dose protocol, we start HMG or urinary FSH on the second or third day of the menstrual cycle then the antagonist is given

daily (0.25 mg) starting on day 7 or 8 of the cycle till the day of HCG injection. In the single dose protocol the drug is given once on the 9th or 10th day of the cycle (3 mg of citrelix).

Notes for the postgraduate

1. GnRH agonist (analogue) pituitary down-regulation protocols give a higher pregnancy rate compared to HMG-only protocol. The long protocols are superior to the short ones.
2. The GnRH antagonists are not better than the GnRH agonists as regards the pregnancy rate. Also the antagonists do not significantly reduce the incidence of severe ovarian hyperstimulation syndrome.
3. There is no significant difference between all gonadotrophin preparations with regards to the rates of ovulation and pregnancy. The difference is only in the cost.

ANTIOESTROGENS

I. CLOMIPHENE CITRATE (CLOMID, SEROPHENE)

Mode of Action

The drug is a synthetic antioestrogen compound. It competes with oestrogen and blocks the oestrogen receptors in the target organs including the hypothalamus. So the hypothalamus is not inhibited by oestrogen and secretes more gonadotrophin releasing hormone which stimulates the pituitary to produce more FSH and LH. So clomiphene needs an intact hypothalamic-pituitary-ovarian axis to induce ovulation. It also blocks oestrogen receptors in the endometrium, cervical glands, and vaginal epithelium.

Indications

1. Infertility caused by anovulation and oligo-ovulation.
2. The polycystic ovary syndrome.
3. Inhibition of lactation after delivery.
4. Treatment of oligospermia in the male.

Contraindication. Liver disease.

Dose

Fifty milligrams daily (one tablet) by mouth for 5 days, starting on the 3rd, 4th, or 5th day of the cycle. If there is amenorrhoea, bleeding is first induced by giving a progestogen. The occurrence of withdrawal bleeding indicates the presence of endogenous oestrogen which is necessary for the action of Clomid. The response to treatment is monitored by recording basal body temperature or measuring serum progesterone (22-24th day of the cycle) or by ultrasound to detect the presence of a ripe follicle, 18 mm or more in diameter. If there is no ovulation the dose is increased by 50 mg every month to reach 250 mg/day. If ovulation occurs treatment is continued for 6 cycles. If no pregnancy occurs after 6 ovulatory cycles, cervical hostility is excluded by postcoital test and laparoscopy is done to exclude other infertility factors. Being antioestrogen, clomiphene makes cervical mucus thick and scanty

(15%) thus interfering with the ascent of spermatozoa. Ovulation occurs 5-10 days after the last tablet of treatment (average 7 days). Human chorionic gonadotrophin (HCG) in a dose of 5000-1000 IU may be given IM after detection of a ripe follicle (18 mm or more in diameter) by ultrasound to trigger ovulation or empirically one week after the last tablet of treatment.

Note. Ovulation-inducing drugs may be associated with increased risk of ovarian cancer. Such a relationship has not been definitely proven. However, it is recommended not to give clomiphene for more than 6 cycles.

Success Rate

Clomiphene induces ovulation in about 75% of cases, but pregnancy occurs in only 50%. This disparity is explained by; (a) effect on cervical mucus and this is treated by giving a small dose of oestrogen from 8th to 12th day of the cycle; (b) ovulation occurs but there is a luteal phase defect, treated by giving HCG IM; (c) luteinization occurs in the graafian follicle but the ovum is not released (LUF syndrome). Treated by a high dose of HCG at midcycle; (d) antioestrogenic effect on the endometrium leading to a decrease in endometrial thickness, maturity, and perfusion. These changes prevent implantation.

Side Effects

1. Ovarian hyperstimulation is rare (2-3%). It is mild and more liable to occur in case of polycystic ovary syndrome and so we start with a small dose (50 mg/day). It is noticed 5-7 days after discontinuation of clomiphene, and is due to increased secretion of LH.
2. Multiple ovulation and multiple pregnancy occurs in 5-10% of cases. Most of the multiple pregnancies are twins (99%).
3. Hot flushes due to antioestrogen effect (10%).
4. Headache (1%).
5. Loss of hair (rare, 0.5%). It is reversible
6. Visual disturbances due to mydriatic effect (1%).
7. Nausea and vomiting.
8. Breast tenderness (2%).
9. Depression.
10. Slight increase in the rate of ectopic pregnancy.

II. TAMOXIFEN (NOLVADEX)

It is an antioestrogen and acts in the same way as clomiphene. Tablet is 10 mg and Nolvadex-D is 20 mg. The dose is 20 mg/day for 5 days starting on the 3rd, 4th, or 5th day of the cycle. The dose can be increased up to 40 mg daily. Some women respond to clomiphene and not to tamoxifen and vice versa. Like clomiphene, it makes the cervical mucus thick and scanty.

Tamoxifen is also used for the treatment of advanced and recurrent endometrial carcinoma and in breast carcinoma.

III. CYCLOFENIL (ONDOGYNE)

It is an antioestrogen and acts in the same way as clomiphene. The tablet is 400 mg. Two tablets are taken daily for 5-10 days starting on the 3rd, 4th, or 5th day of the cycle. Dose can be increased to 4 tablets daily.

ANTIPROGESTOGENS

I. MIFEPRISTONE

It is a 19-nortestosterone derivative. It is antiprogesterone as it blocks the progesterone receptors. It is also antiglucocorticoid as it blocks the glucocorticoid receptors. The trade name is Mifegyna tablets.

Indications

1. Postcoital contraception (the morning-after pill). Progesterone is necessary for implantation of the fertilized ovum. A large dose, 600 mg (12 tablets) is given immediately or within 72 hours after intercourse. The drug blocks progesterone receptors in the endometrium and prevents progesterone action.
2. Abortifacient. It induces abortion in the first trimester.
3. To terminate pregnancy in the second trimester. It is used in combination with extra-amniotic prostaglandin infusion.
4. Treatment of breast cancer. There is evidence that progesterone in addition to oestrogen, stimulates proliferation of breast epithelium, so antiprogesterone therapy may be beneficial in this respect.
5. Treatment of endometriosis.
6. To reduce the size of uterine myomas.
7. Treatment of premenstrual syndrome.
8. Treatment of Cushing syndrome.
9. Treatment of glucocorticoid dependent lymphoma.
10. To treat glaucoma induced by glucocorticoid hormones.
11. To treat meningiomas which frequently show progesterone receptors.

Dose

It is available in 50 milligrams tablets. To induce abortion 4 tablets (200 mg) are given daily for 4 successive days (90% will abort), or a single large dose of 12 tablets (600 mg) is given in combination with a prostaglandin given IM or as vaginal tablet. This causes abortion in 99% of cases.

To terminate pregnancy in the second trimester, 4 tablets (200 mg) are given and after 24 hours we start extra-amniotic prostaglandin infusion. It is more effective than giving prostaglandin alone.

II. GESTRINONE

It is a weak synthetic androgen (a 19-nortestosterone derivative). It leads to amenorrhoea (in 85% of cases) and endometrial atrophy. It has the same action as danazol, but its antiprogestosterone effect is more marked.

Mechanism of Action. As danazol.

Indications. As danazol.

Gestrinone has a long lasting action, and the dose is 1.25-2.5 mg orally twice weekly. It is given for 6-9 months in patients with endometriosis. In case of uterine fibroids it can be given to control bleeding before operation is done.

Side Effects. As danazol.

ANTIANDROGENS

1. Cyproterone acetate (Androcur).
 2. Spironolactone (Aldactone).
 3. Flutamide.
 4. Finasteride.
- } See treatment of hirsutism.

DANAZOL

The drug is a weak synthetic androgen (isoxazol derivative of 17-alpha-ethinyl testosterone). It causes amenorrhoea, anovulation, and endometrial atrophy. The drug is very expensive.

MECHANISM OF ACTION

1. It prevents the midcycle peaks of FSH and LH, but does not inhibit the basal secretion (antigonadotrophin). This prevents ovulation, and produces amenorrhoea.
2. Inhibits the synthesis of steroid hormones in the ovary.
3. Blocks oestrogen and progesterone receptors in the endometrium.
4. Reduces the synthesis of the sex-hormone binding globulin (SHBG) in the liver, so the amount of free testosterone is increased.
5. It displaces testosterone from SHBG thus increasing free testosterone.

The drug has antigonadotrophic, antioestrogenic, antiprogestogenic, androgenic and anabolic effects.

INDICATIONS

1. Endometriosis. The dose is 400-800 mg orally/day in divided doses for 6-9 months.

2. Fibroids. To control bleeding before operation is done.
3. Menorrhagia.
4. Endometrial hyperplasia.
5. Premenstrual syndrome.
6. Fibrocystic disease of the breast (100-400 mg daily in divided doses).
7. Idiopathic precocious puberty (inhibition of FSH, LH secretion).

CONTRAINDICATIONS

(1) Liver disease as it is mainly metabolized in the liver and may cause hepatic damage; (2) hypertension; (3) congestive heart failure; (4) impaired renal function as it can cause fluid retention; (5) pregnancy because of androgenic effects on the female fetus.

SIDE EFFECTS

1. Androgenic effects. Acne, male alopecia, hirsutism, hoarseness of voice which is permanent due to hypertrophy of vocal cords, and hypertrophy of clitoris.
2. Hypo-oestrogenic effects. Hot flushes, sweating and atrophy of the breasts. Atrophic vaginitis, dry vagina, and dyspareunia. Decreased libido.
3. Anabolic effects. Oedema and increase in body weight due to increase in muscle mass.
4. Metabolic effects. Impaired glucose tolerance, increased insulin requirements in diabetic cases, hepatic dysfunction. Blood pressure may be elevated. It decreases high-density lipoprotein cholesterol.
5. Central nervous system. Headache, sleep disorders, anxiety, depression and visual disturbances.
6. Gastrointestinal. Nausea, vomiting and constipation.
7. Musculo-skeletal. Muscle cramps, and swelling of joints.
8. Genitourinary. Haematuria.

LASER THERAPY IN GYNAECOLOGY

Laser is an acronym from the first letters of the words Light Amplification by the Stimulated Emission of Radiation. The laser beam can coagulate, vaporize (ablate) or excise a lesion according to the strength of the beam. It is a form of electromagnetic energy.

TYPES OF LASER

1. Carbon dioxide laser. The main one used in gynaecology.
2. Argon laser.
3. YAG laser (yttrium aluminium garnet or neodymium).
4. KTP 532 laser (potassium tetanyl phosphate).

GYNAECOLOGICAL INDICATIONS

1. **Vulva.** Vulval intraepithelial neoplasia (VIN), basal cell carcinoma, hyperplastic dystrophy with atypia, condylomata acuminata, nevi, urethral caruncle, and to open Bartholin abscess.
 2. **Vagina.** Vaginal intraepithelial neoplasia (VAIN), condylomata acuminata, polyps, vaginal adenosis, and excision of vaginal septum.
 3. **Cervix.** Erosion, conization, cervical intraepithelial neoplasia (CIN), condylomata acuminata, cervical polyps, and to widen stenosed external os.
 4. **Uterus.** To occlude the uterine ends of the tubes as a method of sterilization. Removal of uterine septum. Certain cases of functional menorrhagia to ablate the endometrium and induce amenorrhoea, removal of a fibroid polyp, and resection (shaving) of a submucous myoma (less than 5 cm in diameter). These procedures are done through the hysteroscope.
 5. **Palliative treatment.** In some cases of advanced carcinoma of vulva, vagina or cervix to check the growth of the tumour.
 6. **Rectum.** Condylomata acuminata.
 7. **Penile.** Condylomata acuminata and penile intraepithelial neoplasia.
 8. **Intra-abdominal laser surgery.** The indications include:
 - Ablation (vaporization) of endometriotic lesions.
 - Excision of endometriosis.
 - Ovarian cystectomy.
 - Ovarian drilling in polycystic ovary syndrome.
 - Tubal surgery. Salpingostomy for blocked tubes or ectopic pregnancy, and lysis of adhesions.
 - Removal of adnexa.
 - Myomectomy in selected cases (subserous, and interstitial fibroids).
 - Division of uterosacral ligaments in spasmodic dysmenorrhoea.
 - Ablation of implants from carcinoma of ovary.
- Intra-abdominal laser surgery can be done through the laparoscope i.e. laser laparoscopy.

9. Laser is used as a cutting instrument instead of the knife to open the abdominal wall.

ADVANTAGES OF LASER THERAPY

1. The depth of destruction is under control.
2. Bleeding, fibrosis and infection are less.
3. Rapid healing of the lesion.
4. Less destruction of adjacent tissues compared with electrocautery or cryocautery.
5. Less discharge after treating vulval, vaginal, and cervical lesions.

DISADVANTAGES

1. High cost.
2. Needs special training and experience.
3. Needs precautions to protect the eyes of the operator and medical staff.

CRYOTHERAPY

It is treatment by cooling. Freezing leads to death of the cell and destruction of tissues. Carbon dioxide, nitrous oxide, Freon or nitrogen all in a liquid state are passed through a hollow probe. This will cause drop in temperature (up to -60°C) and freezing of the tissues coming in contact with the cold probe.

GYNAECOLOGICAL INDICATIONS

Cryotherapy (cryosurgery or cryocautery) is used for the treatment of the following lesions:

1. **Cervix.** Chronic cervicitis, erosion, cervical intraepithelial neoplasia (CIN), and condylomata acuminata.
2. **Vagina.** Vaginal intraepithelial neoplasia (VAIN), condylomata acuminata and granulation tissue which may occur in the vaginal vault after total hysterectomy.
3. **Vulva.** Vulval intraepithelial neoplasia (VIN) and condylomata acuminata.
4. **Palliative treatment.** For advanced carcinoma of the cervix, vagina or vulva. It relieves pain, controls bleeding and reduces the offensive discharge.

ADVANTAGES

Bleeding, fibrosis, infection and cervical stenosis are less compared with diathermy or electric cautery.

DISADVANTAGES

1. Prolonged healing time. The cervical lesion takes 8-10 weeks for healing.
2. Excessive vaginal discharge usually continues till healing is complete.
3. Costly.

OPERATIVE GYNAECOLOGY

THE UTERINE SOUND

It is made of a malleable metal, its tip (3-4 mm. in diameter) is blunt to avoid perforation of uterus. It is graduated in inches or centimeters. It is curved to fit in the angle of flexion of the uterus.

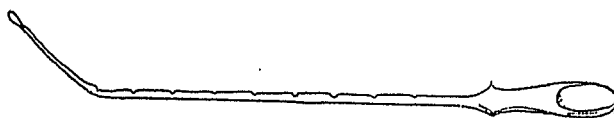


Fig. 120. Uterine sound

INDICATIONS

(1) Diagnosis of cervical stenosis when it cannot be introduced through the cervical canal; (2) to measure the length of the cervix by feeling resistance at the internal os. This is of value to diagnose supravaginal elongation in case of uterine prolapse and during Fothergill operation to estimate the length to be amputated; (3) to measure the length of uterine cavity by feeling resistance at the fundus. This is done before dilatation of the cervix to avoid introducing the dilator for a long distance which may cause perforation of uterus; (4) to diagnose uterine hypoplasia; (5) to know the position and direction of uterus as in case of retroversion; (6) in the presence of a pelvic swelling to know its relation to the uterus; (7) to differentiate between fibroid polyp and inversion of uterus; (8) to differentiate between a polyp arising from the cervical canal or body of uterus; (9) to differentiate between true and false prolapse (congenital elongation of cervix); (10) it may detect an abnormality in the uterus as a polyp or septum; (11) to confirm the presence of intrauterine contraceptive device in the uterus; (12) to test for friability in cancer of cervix (the probe or Clark test); (13) to elicit the click sign in vesicovaginal fistula; (14) diagnosis of incompetent cervix. When the internal os is wide the sound rocks freely inside it and there is absence of a closing snap; (15) it confirms the occurrence of uterine perforation during operation; (16) after healing of the cervix following cauterization, the uterine sound is passed through the internal os to prevent stenosis.

COMPLICATIONS

(1) Shock due to pain may occur in sensitive women; (2) ascending infection; (3) perforation of uterus; (4) abortion may occur if introduced into a pregnant uterus.

N.B.: Uterine hypoplasia is diagnosed when the total length of uterus is less than 6.25 cm (2.5 inches) or when the uterine index is less than 0.75.

$$\text{The uterine index} = \frac{\text{Total length of uterus} - \text{length of cervix}}{\text{Length of cervix}} \times \frac{1}{2}$$

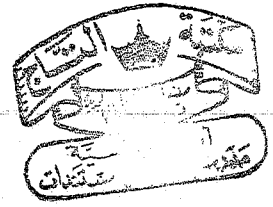
Normally the index is 1 or more than 0.75.

CATHETERIZATION OF THE BLADDER

INDICATIONS

Gynaecological Indications

1. Before vaginal and abdominal operations.
2. Evacuation of the bladder in case of retention of urine.
3. Sterile collection of urine for bacteriological examination.
4. To differentiate between a full bladder and a pelvic or abdominal mass.
5. Diagnosis of vesicovaginal fistula. A metal catheter is passed through the urethra to see its tip from the vagina. The catheter is also used to do the click test and the methylene blue test.
6. Postoperative as in case of repaired vesicovaginal fistula.
7. To differentiate between cystocele and cyst of the anterior vaginal wall.
8. Diagnosis of bladder and urethral injuries.
9. Diagnosis of stone bladder (click sound against a metal catheter).
10. For doing ascending cystogram.



OBSTETRICAL INDICATIONS

1. Before any obstetrical interference as application of forceps, and caesarean section.
2. During labour if the patient is unable to micturate to prevent uterine atony.
3. Atonic postpartum haemorrhage to prevent uterine atony.
4. To help spontaneous correction of incarcerated retroverted gravid uterus.

TYPES OF URINARY CATHETERS

1. Rubber catheters, some types are self-retaining as Foley catheters.
2. Metal catheters (straight and S-shaped used during labour).
3. Plastic catheter (Nelaton).

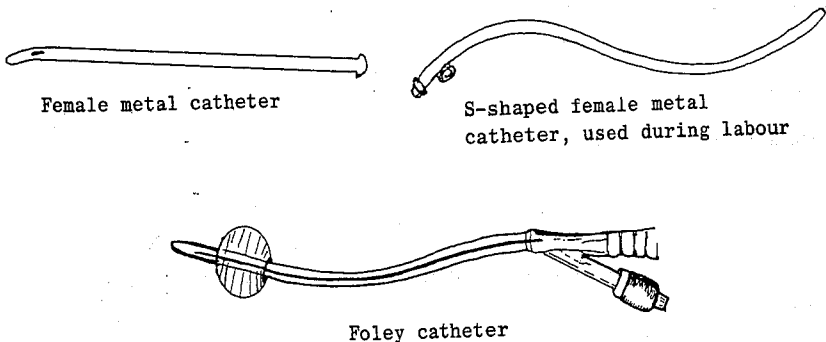


Fig.121. Urinary catheters

DILATATION OF THE CERVIX

INDICATIONS

A. Therapeutic Indications

1. Treatment of spasmodic dysmenorrhoea.
2. Infertility due to cervical stenosis.
3. Drainage of haematometra or pyometra.

B. Dilatation as a Primary Step before other Operations

1. **Operations on the cervix.** Amputation including Fothergill operation, trachelorrhaphy (repair of the cervix), cervical conization and cauterization in the nullipara.
2. **Operations on the uterus.** Evacuation, curettage, polypectomy, before introduction of the hysteroscope, removal of a missed loop and application of radium into the uterus. In case of hysterotomy and caesarean section done before onset of labour, the cervix is dilated abdominally to allow escape of blood and lochia.

TYPES OF CERVICAL DILATORS

Hegar dilator which is of uniform thickness and Fenton dilator which tapers gradually towards the tip. The number on the dilator indicates the diameter in millimeters.

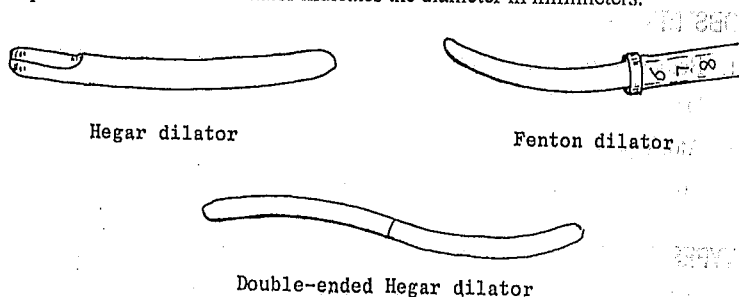


Fig.122. Cervical dilators

THE DEGREE OF DILATATION

This depends upon the indication. The cervix is dilated to No. 7-10 for curettage, No. 12 for amputation of cervix.

TECHNIQUE OF DILATATION

Under general anaesthesia or paracervical block, the patient is placed in the lithotomy position. The vulva, vagina and perineum are painted with an antiseptic solution and sterile towels are applied. The bladder is evacuated by a catheter and the patient is examined bimanually under anaesthesia to determine the position, size, shape, and consistency of the uterus and any other abnormality. The cervix is exposed by applying a self-retaining posterior vaginal speculum (Auvard speculum). The anterior lip of the cervix is grasped with a vulsellum and pulled downwards. The cervix is painted with iodine and a uterine sound is passed to determine the length and direction of the uterus. The cervix is gradually dilated

starting with the smallest dilator (No. 3). The dilator is grasped in the hand like a pencil with the index finger placed at the exposed length to enter the uterus. The dilator is introduced into the cervix until it passes the resistance of the internal os. The dilator is left in place for half a minute to allow relaxation of the smooth muscle fibres of the cervix. The dilator is removed and a larger one is introduced until the cervix is dilated to the desired extent.

COMPLICATIONS OF DILATATION

1. Neurogenic shock if light anaesthesia is used.
2. Perforation of uterus or cervix by the uterine sound, dilator or curette. It is avoided by passing the uterine sound at first to measure the length of the uterus so that the dilator is not introduced for a long distance, also the dilator is grasped in the hand like a pencil. Perforation occurs in about 6 in 1000 cases.
3. Ascending infection as salpingitis, peritonitis and parametritis.
4. Cervical laceration and this may lead to haemorrhage, cervicitis or incompetent cervix with recurrent abortion or preterm labour. Laceration is more liable to occur if the cervix is dilated more than 12 mm.
5. Secondary haemorrhage may occur 7-10 days later due to separation of a necrotic slough.
6. Anaesthetic complications.

N.B.: Perforation of the uterus is treated conservatively by keeping the patient under observation for vital signs and giving antibiotics. However, if there is internal haemorrhage, uterine infection or malignant disease, laparoscopy is performed to confirm the diagnosis and laparotomy is done followed by repair of uterus or hysterectomy according to the findings. When a pregnant uterus is perforated during evacuation, laparoscopy is done by a second operator to allow evacuation of the uterus under laparoscopic vision or under ultrasound guide.

TRACHELORRHAPHY (REPAIR OF THE CERVIX)

1. **Emmet trachelorrhaphy.** Indicated for a lacerated non-hypertrophied cervix. The cervix is dilated to No. 12 Hegar and the edges of the laceration are excised including the apex of the tear, then the raw areas are sutured together by interrupted chromic catgut or delayed-absorbable stitches as Vicryl or Dexon.
2. **Bonney trachelorrhaphy.** Indicated for a lacerated hypertrophied cervix. It is partial amputation of the cervix. The cervix is dilated and a circular incision is made in the vaginal mucosa reaching above the tear. The mucosa is dissected upwards from the anterior and posterior lips and the cervix is amputated. The vaginal mucosa is brought down to cover the raw area of the cervix.

UTERINE CURETTAGE

INDICATIONS

A. Diagnostic Indications

(1) Diagnosis of malignant disease of the endometrium or endocervix; (2) diagnosis of diseases of the endometrium as bilharziasis and tuberculosis; (3) diagnosis of dysfunctional uterine bleeding; (4) to detect ovulation in case of infertility; (5) to investigate a case of amenorrhoea.

B. Therapeutic Indications

(1) After evacuation to remove the decidua; (2) postabortive and postpartum haemorrhage to remove retained products of conception; (3) removal of endometrial and endocervical polyp; (4) dysfunctional uterine bleeding to arrest haemorrhage; (5) membranous dysmenorrhoea; (6) removal of congested endometrium during Fothergill operation; (7) removal of a loop fragmented inside the uterus; (8) to divide adhesions in Asherman syndrome.

C. Before insertion of radium to induce artificial menopause to exclude an early malignant lesion in the endometrium which may be stimulated by the relatively small castration dose.

TYPES OF UTERINE CURETTES

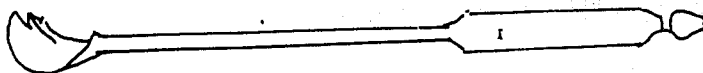
(1) Sharp uterine curette; (2) blunt uterine curette. It is used when the uterus is soft as in case of malignant disease of the uterine body, evacuation, postabortive bleeding, secondary postpartum haemorrhage and senile endometritis; (3) combined sharp and blunt uterine curette; (4) blunt flushing curette "Rheinstadter" which was previously used during evacuation to curette and at the same time to wash the uterine contents with a warm antiseptic solution; (5) fundal curette to curette the fundus, angles and lateral walls; (6) biopsy curette which is used to detect ovulation in case of infertility. It is used without anaesthesia because it can be introduced without dilatation of the cervix; (7) suction curette used for suction evacuation to terminate pregnancy, to remove retained products of conception, and for evacuation of hydatidiform mole.

TECHNIQUE OF DILATATION AND CURETTAGE

Under anaesthesia the cervix is dilated until the curette can be passed (7-10 Hegar). A polyp forceps is used to explore the uterine cavity to remove any endometrial polyp. The curette is then introduced to reach the fundus and the endometrium is removed from above downwards starting with the anterior then the posterior wall. Fundus, angles, and lateral walls are scraped by the fundal curette or the endometrial cavity is curetted in a clockwise direction. Curettage is continued until a gritty sensation is felt or heard. This means that we have reached the basal layer of the endometrium which should not be removed to allow for regeneration of the endometrium. The material obtained is preserved in 4% formalin solution or 95% alcohol for histological examination.



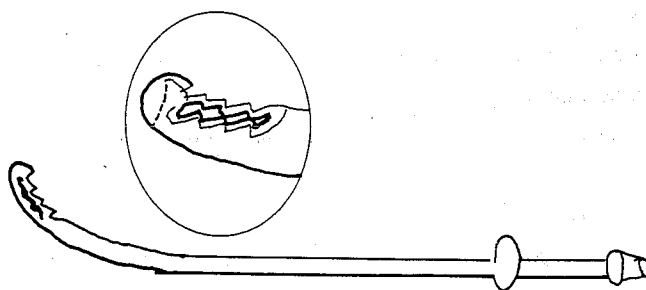
Combined blunt and sharp curette (Sims)



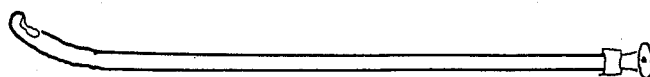
Blunt flushing curette (Rheinstadter)



Fundal curette



Biopsy curette (Novak)



Biopsy curette (Randall)

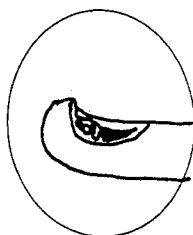


Fig.123. Uterine Curettes

COMPLICATIONS OF CURETTAGE

1. Complications of dilatation.
2. Permanent amenorrhoea due to removal of basal layer of endometrium.
3. Asherman syndrome and secondary amenorrhoea due to formation of intrauterine adhesions.
4. Endometriosis. Endometrial tissue may be implanted in a vaginal or perineal scar, giving rise to endometriosis.

Fractional Curettage. See cervical carcinoma.

CERVICAL CONIZATION

INDICATIONS

1. For diagnosis of cervical intraepithelial neoplasia (CIN). See page 233.
2. Treatment of CIN III and resistant cases of CIN II and CIN I.
3. Treatment of some cases of chronic cervicitis when the endocervix and portio vaginalis are markedly affected by infection and laceration.

TECHNIQUE

Conization is done under general anaesthesia using a cold knife (scalpel) or a special loop or laser. Haemostatic sutures are placed at 3 and 9 o'clock positions to reduce bleeding from the cervical branch of the uterine artery. Also dilute vasopressin (10 IU in 100 ml sterile saline) is injected into the cervical stroma to reduce bleeding. A circular incision is made around the external os including all abnormal areas on the portio vaginalis. These are determined by the colposcope or Schiller iodine test. The incision is deepened so that the apex of the cone reaches just below the anatomical internal os to include the whole endocervical epithelium. A suture is applied at 12 o'clock position to identify the different parts of the specimen. The raw area left after conization is not covered with cervical mucosa as this reduces the incidence of cervical stenosis, and allows any remaining malignant cells to be detected by the cervical smear during the follow-up of the case. The cone is divided into many serial sections (about 75) for microscopic examination.

Note. The posterior part of the cone (3 to 9 O'clock) is usually incised first so that bleeding will not obscure the operative field.

COMPLICATIONS. See page 234.

Note. Cervical conization is done during pregnancy if microinvasion is diagnosed or suspected by cervical smear, colposcopy, or punch biopsy.

TUBAL INSUFFLATION (RUBIN TEST)

The method was used in the past to detect tubal patency. It is now replaced by hysterosalpingography. Air or carbon dioxide was injected into the uterus by a special cannula using the Bonney insufflation apparatus.

HYSTEROSALPINGOGRAPHY (HSG)

INDICATIONS

1. To investigate primary and secondary infertility.
2. Before and after myomectomy to detect tubal patency.
3. Before and after salpingoplasty to detect tubal patency.
4. After operation for tubal pregnancy to examine patency of the other tube.
5. Diagnosis of congenital anomalies of the uterus.
6. Diagnosis of incompetent cervix. Isthmography will show a funnel-shaped cervix.
7. In the presence of a pelvic swelling to know its relation to the uterus.
8. Diagnosis of intrauterine synechiae.
9. Irregular uterine bleeding to exclude an organic cause as uterine polypi.
10. To know if a missed intrauterine device is inside or outside the uterus.
11. To assess the scar of a lower segment caesarean section.

As regards the technique, contraindications and complications, see infertility.

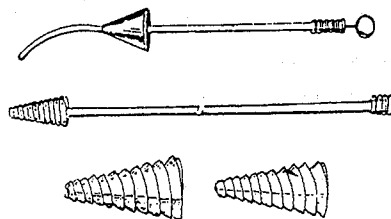


Fig. 124. Cannula for hysterosalpingography.

GYNAECOLOGICAL ENDOSCOPY

The different procedures of gynaecological endoscopy include:

1. Colposcopy.
2. Hysteroscopy.
3. Laparoscopy.
4. Tuboscopy.
5. Cystoscopy.
6. Proctoscopy and Sigmoidoscopy.

COLPOSCOPY

The colposcope is a stereoscopic binocular microscope which allows magnification of 10 to 40 times. In routine practice a magnification of 16 is used. In this way we can study lesions which are not seen by the naked eye and select the site of biopsy from abnormal areas.

INDICATIONS

1. Examination of the cervix when the cervical smear is abnormal.
2. Examination of a clinically suspicious cervix even if the cervical smear is negative for malignant cells.
3. Follow-up of patients treated for cervical intraepithelial neoplasia.
4. Evaluation of abnormal lesions in the vulva and vagina.

PROCEDURE

1. Done without anaesthesia.
2. Patient placed in lithotomy or dorsal position.
3. Cusco speculum to expose the cervix.
4. Focus the lens.
5. Clean the cervix with normal saline to remove mucoid secretion. Examine the cervix to see any area of leucoplakia (white patch) or any other pathology.
6. Dilute acetic acid solution (2-5%) is applied, wait for 5 minutes then the cervix is reexamined.
7. The normal squamous epithelium covering the portio vaginalis appears smooth and pink. The columnar epithelium of cervical canal is a red papillary surface and grape-like in appearance. The transformation zone which is the junction between the columnar and squamous epithelium shows areas of columnar epithelium, tongues of immature squamous epithelium (metaplastic squamous epithelium), gland openings and nabothian follicles. Cervical carcinoma always starts at or near the transformation zone.
8. A green filter can be used which allows better visualization of the blood vessels which appear black.
9. A camera can be attached to the colposcope for photography.
10. Punch biopsy is taken from suspected areas. The cervical canal is curetted to exclude an endocervical lesion. Specimens are sent for histopathology to confirm the diagnosis.
11. The colposcopic findings are recorded on a special format.

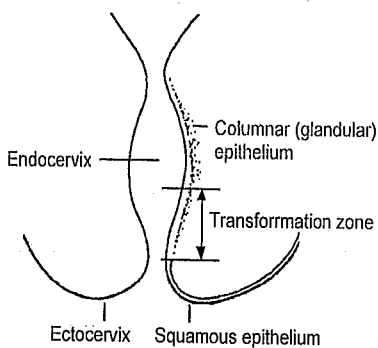
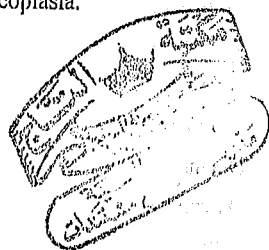


Fig. 125. Transformation zone

Notes

- Immature or metaplastic squamous epithelium does not contain glycogen. It results from proliferation of the reserve or basal cells normally found beneath the columnar epithelium lining the cervical canal. This proliferation is stimulated by vaginal acidity.
- Pain only occurs when the cervix is dilated, so for colposcopic examination anaesthesia is not necessary.

I. NORMAL COLPOSCOPIC FINDINGS

- A. Original (native) squamous epithelium. It is the normal squamous epithelium found on the portio vaginalis.
- B. Columnar epithelium lining the cervical canal.
- C. Typical (normal) transformation zone.

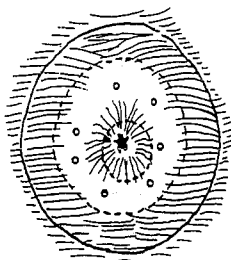


Fig.126. Transformation zone



Fig.127. Mosaic area

II. ABNORMAL COLPOSCOPIC FINDINGS

- A. Atypical (abnormal) transformation zone.

It shows the following lesions:

1. Leucoplakia.
2. Acetowhite epithelium (white patches seen by the colposcope after application of acetic acid).
3. Mosaic areas. Polygonal white areas separated by red lines due to the presence of newly formed capillaries which run beneath the surface epithelium.
4. Punctuation. Red stippling (spots) resulting from light reflected from capillary loops growing perpendicular to the surface. They are seen end-on as a dot.
5. Abnormal blood vessels. Comma-like, spaghetti-like, corkscrew and hair-pin vessels.
Normal blood vessels branch like a tree.

- B. Suspicion of invasive carcinoma. The tissues show raised edge, with irregular contour and abnormal blood vessels.

III. UNSATISFACTORY COLPOSCOPIC FINDING

The whole squamocolumnar junction (transformation zone) or the whole lesion cannot be visualized.

Notes

- Leucoplakia. A white patch seen by the naked eye before application of acetic acid. It is a layer of keratin. It may or may not be associated with abnormal cells.
- Acetowhite epithelium. Acetic acid withdraws water from cells and areas with a high nuclear density become white in colour.

HYSTEROSCOPY

The hysteroscope is a telescope with a diameter of 4 or 10 mm which is inserted transcervically to allow visualization of the uterine cavity. The cavity is distended with carbon dioxide, 5% dextrose in water, glycine, sorbitol, or 32% dextran solution (Hyskon). The latter does not mix with blood and this improves the visual field. The hysteroscope consists of a telescope and an outer sheath. The telescope contains a fiberoptic light source and an optic system for transmitting the image. The outer sheath contains a channel for the introduction of the distending medium and a channel for instruments as biopsy forceps, scissors, and for laser beams. The hysteroscopes give a magnification of "no magnification", 20, 60, and 150.

The diagnostic hysteroscope has a diameter of 4 mm and so used without anaesthesia. The operative hysteroscope has a diameter of 10 mm and so needs cervical dilatation done under general or local paracervical anaesthesia.

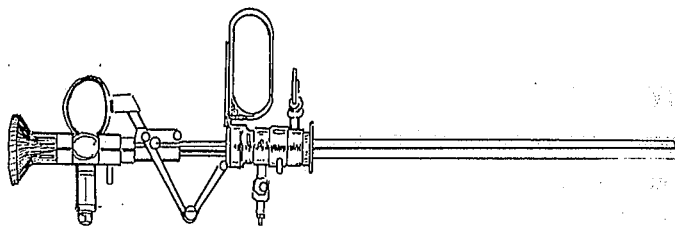


Fig.128. The hysteroscope

INDICATIONS OF HYSTEROSCOPY**A. Diagnostic Hysteroscopy**

The hysteroscope is used for the diagnosis of:

1. Abnormal uterine bleeding.
2. Intrauterine adhesions.
3. Endometrial polypi.
4. Submucous fibroid.
5. Missed intrauterine device.
6. Congenital uterine anomalies as septate uterus.
7. Retained products of conception.
8. Small endometrial carcinoma missed by dilatation and curettage, and to determine the extent of the lesion to the cervical canal to plan surgery.



9. Microhysteroscopy to examine the transformation zone when it lies inside the cervical canal and cannot be seen by the colposcope. The microhysteroscope is used to examine with a magnification of 60 and 150.

B. Operative hysteroscopy

It is used for:

1. Division of intrauterine synechiae.
2. Removal of endometrial polypi.
3. Removal of a fibroid polyp and resection of a submucous fibroid less than 5 cm in diameter. Any remaining part may be expelled spontaneously through the cervix after 2-3 weeks or resection is repeated.
4. Removal of a missed loop.
5. Resection of a uterine septum.
6. Endometrial ablation in case of dysfunctional menorrhagia when the patient is unfit for hysterectomy or refuses operation (see endometrial ablation).
7. Treatment of infertility. Intrauterine insemination or embryo transfer in patients with uterine abnormality as bicornuate uterus. Tubal insemination and transuterine GIFT procedure (gamete intrafallopian transfer). Also transcervical balloon dilatation in proximal tubal obstruction.
8. Sterilization by occluding the uterine ends of the tubes by cauterization, laser, chemicals as silver nitrate, silicon plugs, or insertion of intratubal device.

CONTRAINDICATIONS

1. If pregnancy is suspected.
2. Pelvic infection (in vagina, cervix, uterus, or tubes).
3. During menstruation and heavy bleeding as blood masks the visual field and there is a possibility of air embolism (relative contraindication).
4. Sensitivity to anaesthetic or distension medium.
5. Lack of proper equipment.
6. Lack of experience.

COMPLICATIONS

1. Perforation of uterus.
2. Haemorrhage during resection of a septum, polyp, or fibroid.
3. Infection.
4. Complications due to absorption of the fluids used to distend the uterus in the form of pulmonary embolism, cerebral oedema, hypertension, dilutional hyponatraemia and dilutional coagulopathy.
5. Anaesthetic complications.

Note. Hyskon is 32% dextran with molecular weight 70,000 in 10% dextrose (Dextran 70). In contact hysteroscopy, no fluid medium is used, and the hysteroscope is inserted directly into the undistended uterine cavity. The lens must touch the observed areas.

LAPAROSCOPY

INDICATIONS

A. Diagnostic Indications

1. Infertility. Laparoscopy is indicated if no cause of infertility is detected by the routine investigations and if no pregnancy occurs 6 months after treatment of anovulation. It is also indicated when the hysterosalpingogram is abnormal. The laparoscope can reveal peritubal adhesions, fimbrial phimosis (narrow ostium), pelvic endometriosis and tuberculosis, cystic ovaries and uterine malformation as bicornuate uterus. A biopsy can be taken from the ovary or the tube. When laparoscopy is performed at the proper time in the menstrual cycle, it detects the occurrence of ovulation by demonstrating a fresh corpus luteum in the ovary.
2. In primary amenorrhoea to study the ovaries and biopsy may be taken.
3. To diagnose polycystic ovary syndrome.
4. Irregular uterine bleeding and postmenopausal bleeding to exclude a small oestrogenic ovarian tumour.
5. Diagnosis of adnexal mass.
6. Diagnosis of ectopic pregnancy.
7. Diagnosis of pelvic endometriosis.
8. Before tuboplasty to plan the technique to be used.
9. Second look after tuboplasty or treatment of endometriosis.
10. Patients with unexplained chronic pelvic pain.
11. Evaluation of uterine perforation.
12. Pelvic injuries after penetrating or nonpenetrating abdominal trauma.
13. Disorders of the liver, e.g. neoplasia, cirrhosis and splenomegaly.
14. Staging of Hodgkin disease and lymphomas.

B. Therapeutic Indications (Operative Laparoscopy)

1. Tubal surgery.
 - a. Tubal sterilization by diathermy coagulation or application of clip or ring. It is the most common indication for therapeutic laparoscopy.
 - b. Treatment of ectopic pregnancy.
 - c. Division of pelvic adhesions in case of infertility.
 - d. Salpingostomy for fimbrial phimosis.
 - e. Salpingectomy.

2. Ovarian surgery
 - a. Ovarian drilling in polycystic ovary syndrome using electrocauterization or laser.
 - b. Ovarian cystectomy.
 - c. Ovariectomy.
 - d. Aspiration of a small unilocular ovarian cyst.
3. Uterine surgery
 - a. Myomectomy in selected cases.
 - b. Hysterectomy and laparoscopically assisted vaginal hysterectomy.
 - c. Ventrosuspension of a retroverted uterus.
4. Removal of intrauterine device that perforated the uterus.
5. Destruction of foci of endometriosis by diathermy coagulation or laser vaporization and excision of endometrioma.
6. Presacral neurectomy in spasmodic dysmenorrhoea.
7. Division of uterosacral ligaments using laser in spasmodic dysmenorrhoea.
8. Lymphadenectomy.
9. GIFT procedure (gamete intrafallopian transfer).
10. Biopsy of tumour, liver, ovary, spleen, omentum, etc.

CONTRAINDICATIONS

A. Absolute Contraindications

1. Conditions associated with a high risk of visceral injury.
 - Generalized peritonitis.
 - Paralytic ileus.
 - Intestinal obstruction.
 - Severe intraperitoneal haemorrhage.
 - Large hepatosplenomegaly.
 - Large pelvi-abdominal mass.
 - Advanced pregnancy (>16 weeks).
2. When pneumoperitoneum is contraindicated.
 - Diaphragmatic hernia.
 - Large abdominal wall hernia.
3. Coagulation disorders.

B. Relative Contraindications

- Severe cardiac or pulmonary disease.
- Excessive obesity.
- Previous extensive abdominal surgery or previous multiple laparotomies as the bowel may be adherent to the scar. Open laparoscopy is preferred in these cases.
- Previous history of bowel injury.

ANAESTHESIA

General anaesthesia is used in most cases. However, other types of anaesthesia as local, spinal, epidural and acupuncture anaesthesia can be used.

SURGICAL TECHNIQUE

- Patient is put in modified lithotomy position. The thighs are slightly flexed (45°) and slightly abducted to allow free movements of the instruments. The buttocks should hang over the edge of the table to facilitate vaginal and abdominal manipulations.
- The abdomen, vulva, vagina and perineum are cleaned and draped.
- Bladder is evacuated by a catheter, if the patient did not empty the bladder before the procedure.
- Bimanual examination is done to feel the uterus and adnexa.
- A speculum is inserted to expose the cervix.
- The anterior lip of cervix is grasped with a vulsellum.
- A uterine sound is passed to estimate the length of the uterus and its direction.
- A uterine cannula (Rubin, Cohen, or Jarcho) is inserted into the cervical canal and fixed to the vulsellum so that it can be used as a "handle" to move the uterus in different directions during visualization of the pelvis.
- A 1-cm transverse incision is made within or immediately below the umbilicus to cut the skin and subcutaneous fat. The abdominal wall above the symphysis pubis is elevated upward with the left hand and a Veress needle is passed through the incision and after piercing the posterior layer of the rectus sheath, the needle is advanced at 45° -degree angle in the direction of the pelvic cavity to reach the peritoneal cavity.
- Carbon dioxide is introduced and the intra-abdominal pressure is recorded. It should not exceed 20 mmHg. 2-4 litres are usually enough to insufflate the abdomen. If the pressure is above 20 mmHg it indicates extraperitoneal placement of the gas.
- The needle is withdrawn and a trocar and cannula inserted through the abdominal wall at a 45° -degree angle, with the tip pointed toward the pelvis. The trocar is removed and the laparoscope is inserted. The fiberoptic light cable is connected to the laparoscope also the cable which transmits carbon-dioxide is attached to the cannula to allow the entry of a constant rate of the gas to maintain a good pneumoperitoneum.
- Now place the patient in the Trendelenburg position.
- The assistant or the examiner moves the uterine cannula so that the pelvic organs can be inspected. A second puncture in the suprapubic region or iliac fossa is sometimes necessary to allow proper inspection. For operative laparoscopy a second or more puncture is done to allow introduction of instruments.
- To test for tubal patency, methylene blue solution is injected through the uterine cannula to see leakage of the dye from the fimbrial ends.

- At the end of the procedure the laparoscope is removed and air in the abdomen is allowed to escape through the cannula which is finally removed.
- Skin incision is closed using a clip or subcuticular stitch.
- The findings are recorded on a special form.

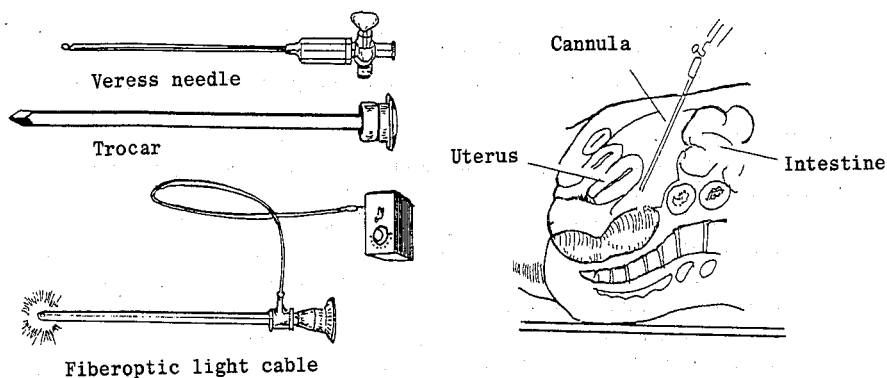


Fig.129. Laparoscopy

COMPLICATIONS

1. Injury of the bowel and other abdominal organs.
 2. Perforation of uterus by the sound or trocar and cannula.
 3. Haemorrhage due to injury of inferior epigastric vessels in the abdominal wall, omental vessels, iliac vessels even aorta or inferior vena cava.
 4. Infection of the abdominal wound and peritonitis.
 5. Emphysema of the abdominal wall.
 6. Gas embolism when Veress needle enters a large blood vessel.
 7. Burning of the abdominal wall and bowel if diathermy is used as in case of tubal sterilization.
 8. Omental hernia at the puncture site.
 9. Cardiovascular complications in the form of hypotension, cardiac arrhythmias and cardiac arrest. The increased intraperitoneal pressure (a) reduces venous return leading to hypotension; (b) increases vagal stimulation; (c) leads to hypercarbia and acidosis causing cardiac arrhythmias. Cardiac arrest may occur due to hypotension, increased vagal stimulation, hypercarbia, and gas embolism.
 10. Anaesthetic complications.
- Complication rate is 0.3 to 3.5% and mortality rate about 0.05%.

TIMING OF LAPAROSCOPY

Laparoscopy is done in the postmenstrual phase and before ovulation to avoid the possibility of preventing implantation of a fertilized ovum, or causing early abortion.

However, if it is done in the second half of the menstrual cycle, it can detect the presence of a corpus luteum to confirm ovulation and allows endometrial biopsy to diagnose luteal phase defect, and to exclude endometrial pathology as tuberculous endometritis.

Notes

- Failed laparoscopy can occur in massively obese patient, as the Veress needle may not enter the peritoneal cavity to induce pneumoperitoneum.
- Anaesthetic complications are the most common cause of death during laparoscopic sterilization.

Notes for the postgraduate

- The most common complaint after laparoscopy is shoulder pain secondary to sub-diaphragmatic accumulation of gas.
- Open laparoscopy. A small incision is made in the abdominal wall and the peritoneum is opened under direct vision. The cannula is placed in the peritoneal cavity and Allis forceps or a purse string suture is used to make an airtight seal. Insufflation is performed through the cannula to create the pneumoperitoneum.
- The following tests indicate that Veress needle is inside the peritoneal cavity.
 1. Snap test. Feeling the snap of the needle as it passes through posterior layer of rectus sheath.
 2. Free movement of the needle in all directions. This procedure is not recommended as it may convert a small needle injury to the bowel into a large one.
 3. Hanging drop test. A drop of saline is placed in the proximal end of the needle and the abdominal wall is elevated. The drop will disappear because of the negative intra-abdominal pressure.
 4. Syringe test (Palmer test). 5 ml of saline are injected by a syringe in the needle and then aspirated. If saline returns to the syringe it indicates that the needle is extraperitoneal.
 5. Observation of intra-abdominal pressure. If it exceeds 20 mmHg, it means presence of the gas in extraperitoneal tissues.
 6. Loss of liver dullness after the passage of one litre of CO₂ into the peritoneal cavity reassures that the needle is inside.
- Palmer point. It is on the midclavicular line, 3 cm below the left costal margin. Some recommend the insertion of a minilaparoscope (diameter less than 2 mm) at the Palmer point in women with previous laparotomy to diagnose the presence of adhesions before insertion of Veress needle. Splenomegaly should be excluded before the procedure. Open laparoscopy is an alternative if we suspect intraperitoneal adhesions.

TUBOSCOPY

The salpingoscope and falloscope allow direct inspection of the lumen of the fallopian tube and study of the anatomy and physiology of tubal mucosa. They also show the presence of debris which may be responsible for tubal obstruction. The salpingoscope is introduced through the fimbrial opening of the tube using the laparoscope. The falloscope which is malleable is introduced through the uterine opening of the tube using the hysteroscope. Tuboscopy has a role in case of unexplained infertility and abnormal salpingography. Damaged tubal mucosa can lead to infertility in spite of tubal patency.

CYSTOSCOPY

It is used to detect involvement of the urinary bladder in case of malignant tumour of the vulva, vagina, cervix and body of uterus.

Bullous oedema is caused by obstruction of the lymph vessels by the growth, and is considered the earliest indication of bladder involvement. Ridges and furrows into the bladder wall are signs of submucous involvement.

All bladder and ureteric fistulae should be investigated by cystoscopy (see genitourinary fistulae).

Cystoscopy is used to differentiate between stress incontinence and detrusor overactivity. It should be done before starting treatment for detrusor overactivity to exclude calculi, infection, polyps, tumours, and diverticulae.

PROCTOSCOPY AND SIGMOIDOSCOPY

The proctoscope and sigmoidoscope are used to evaluate cases presenting with rectal bleeding, tenesmus, blood-stained mucus, and dyschezia to exclude malignant lesions and endometriosis.

MYOMECTOMY

DEFINITION

INDICATIONS

See Treatment of Fibroids

CONTRAINDICATIONS

TYPES

1. Abdominal myomectomy.
2. Vaginal myomectomy.
3. Laparoscopic myomectomy.
4. Hysteroscopic myomectomy.

PREOPERATIVE EVALUATION

1. Complete history and physical examination.
2. Complete blood count. Haemoglobin should not be less than 11 gm%. A patient with a normal haemoglobin level can have 2 units of her own blood obtained 2 weeks before surgery and stored, while she receives iron treatment. Blood is used for autologous donation.
3. Ultrasonography if not already done.

4. Endometrial biopsy or uterine curettage is done if there is irregular uterine bleeding to exclude endometrial carcinoma.
5. If infertility is a complaint, all investigations of infertility including hysterosalpingography are carried out to exclude another cause of infertility and to confirm tubal patency.
6. Hysteroscopy may be used to diagnose a submucous fibroid or a small fibroid polyp.
7. Intravenous pyelogram is done in case of cervical and broad ligament tumour to show the course of the ureter, to diagnose hydronephrosis and to assess kidney function.
8. Other investigations to prepare the patient for operation.
9. A written consent for hysterectomy should be obtained from the patient and husband as hysterectomy may be needed during operation.

METHODS TO REDUCE BLOOD LOSS DURING MYOMECTOMY

A. Preoperative Measures

1. Correction of anaemia. Haemoglobin should not be less than 11 gm%.
2. If patient is taking Aspirin it should be stopped at least 2 weeks before operation.
3. A gonadotrophin releasing hormone analogue may be given for 3 months before operation. It corrects anaemia by causing amenorrhoea. It reduces the size and vascularity of the myomas and so the operation becomes easier and with less blood loss.
4. Operation is done in the postmenstrual period when there is no pelvic congestion.

B. Measures during Operation

1. Anaesthetics that cause uterine relaxation are better avoided.
2. An ampoule of ergometrine (0.25 mg) may be given intravenously at the start of operation.
3. Injection of vasopressin (pitressin) in the uterine wall at the site of incisions (one ampoule 20 units diluted with 20 ml normal saline or Ringer lactate solution).
4. The use of Bonney myomectomy clamp or a rubber catheter to surround the lower part of the uterus to compress the uterine arteries to minimize blood loss.
5. The use of ring forceps to occlude the ovarian arteries in the infundibulopelvic ligaments.
6. The use of a vertical incision in the midline which is the least vascular area.
7. Minimize the number of incisions in the uterus.
8. Removal of the tumour through the proper plane within its capsule.

TECHNIQUE OF ABDOMINAL MYOMECTOMY

- The abdomen is opened by a midline subumbilical incision reaching just above the upper border of symphysis pubis or by a transverse suprapubic (Pfannenstiel) incision.
- After exploration, the uterus is delivered out of the wound.
- A Bonney myomectomy clamp or a rubber catheter is applied to surround the lower part of the uterus to compress the uterine arteries to minimize blood loss during operation. A ring forceps may also be applied to each infundibulopelvic ligament. Ergometrine can be given IV at the start of operation or vasopressin (pitressin) may be injected into the uterine wall.

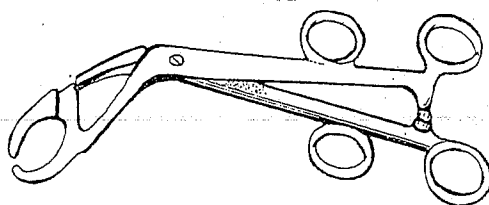


Fig.130. Bonney myomectomy clamp

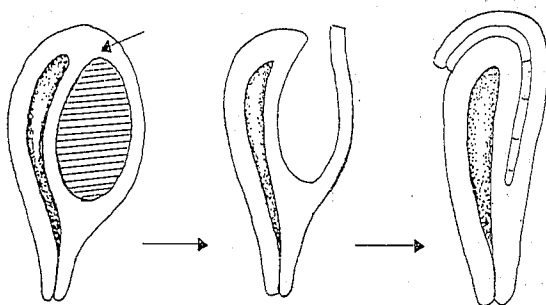


Fig.131. Bonney hood technique

- The uterine wall is incised and the myoma is removed from its capsule using traction with the vulsellum or myoma screw.
- In case of multiple tumours, the incision is made to remove the maximum number through the same incision, and small tumours can be removed by tunnelling.
- The best incision is in the midline of the anterior wall of the uterus to minimize bleeding and to avoid postoperative adhesions to the omentum and intestine. For the last reason, a posterior wall fibroid is removed by a transcavitary incision, or by Bonney hood technique, where a transverse incision is made in the fundus just away from the fallopian tubes, the flap is dissected downward to remove the tumour and then the redundant flap (hood) is brought forward over the fundus and sutured to the anterior wall. In some cases the posterior wall fibroid is removed by a direct incision over the tumour.
- The uterine cavity is not opened to avoid formation of intrauterine adhesions, however, if there is a submucous fibroid the cavity is opened to remove the tumour.
- The cavities are obliterated by chromic catgut or delayed-absorbable sutures as Vicryl. The peritoneal coat is closed with thin delayed-absorbable sutures to minimize adhesions (5/0 Vicryl).
- Finally the clamp or rubber catheter is removed and the uterus inspected to be sure of haemostasis.
- The round ligaments are plicated or sutured together in front of the uterus to prevent retroversion and postoperative adhesions between the intestine and anterior wall of uterus. Plication of uterosacral ligaments also prevents retroversion.

- Before abdominal closure, Dextran solution, or Ringer lactate solution may be instilled in the peritoneal cavity to prevent postoperative adhesions.
- Antibiotics must be given after surgery.

COMPLICATIONS OF MYOMECTOMY

I. During Operation

1. Primary haemorrhage.
2. Injury to the bladder, ureter, fallopian tubes, and intestine.
3. Anaesthetic complications as Mendelson syndrome due to aspiration of vomitus.

II. Postoperative Complications

1. Cardiovascular. Reactionary and secondary haemorrhage, venous thrombosis and pulmonary embolism.
2. Pulmonary. As bronchitis, pneumonia, and lung atelectasis.
3. Gastrointestinal tract. Postoperative distension, vomiting, acute gastric dilatation, paralytic ileus and peritonitis. Later adhesions and intestinal obstruction. Myomectomy is associated with bleeding, and traces of blood left in the peritoneal cavity predispose to slow recovery of intestinal movements.
4. Complications in the abdominal wound. Infection, burst abdomen, keloid formation and incisional hernia. Incisional hernia is very rare after Pfannenstiel incision (1 in 1250 cases).
5. Intrauterine adhesions (Asherman syndrome) if the uterine cavity is opened.
6. Persistence of menorrhagia (1-5%) due to missed fibroids, endometrial hyperplasia, cystic changes in the ovaries, or if redundant tissue is not removed and the uterus is left bulky.
7. Recurrence of fibroids in 10-25% of cases within 10 years due to missing small fibroids at operation, or the growth of new tumours.
8. Rupture of the uterine scar in subsequent pregnancy or labour.
9. Endometriosis due to implantation of endometrial tissue in the pelvis or abdominal wound. This is liable to occur if the uterine cavity is opened during operation.

Note. If the uterine cavity is opened or there is extensive dissection of the myometrium, caesarean section is indicated in subsequent delivery.

VAGINAL MYOMECTOMY

It is indicated for a small fibroid polyp not larger than 8 weeks pregnancy. The tumour is grasped by a vulsellum and twisted until the pedicle tears. The bleeding is usually slight or absent. If the pedicle is thick it is cut with scissors. A large polyp can be removed vaginally by cutting it piece-meal (morcellation) or after doing vaginal hysterotomy (the bladder is dissected upwards then the anterior wall of the cervix is divided to be able to remove the tumour).

LAPAROSCOPIC MYOMECTOMY

The laparoscope can be used to remove subserous and interstitial fibroids, up to 10 cm in diameter, but not submucous tumours. Also during laparotomy or laparoscopy, carbon dioxide laser can be used to vaporize small fibroids and excise moderate and large tumours.

HYSTEROSCOPIC MYOMECTOMY

A fibroid polyp inside the uterine cavity can be removed by the operative hysteroscope. A submucous myoma less than 5 cm in diameter is resected (shaved) by the diathermy loop of the hysteroscope (resectoscope). Any remaining part may be expelled spontaneously through the cervix after 2-3 weeks or resection is repeated. YAG laser through the hysteroscope can deal with these lesions. The tumour is excised or multiple passes are made through its substance to destroy the blood supply leading to its necrosis. Hysteroscopic myomectomy avoids abdominal and uterine incisions and shortens hospital stay.

Note. Myomectomy has a higher mortality rate than hysterectomy because of the risk of haemorrhage which may occur from the tumour bed.

HYSTERECTOMY

INDICATIONS

I. Obstetric Indications

1. Uncontrollable postpartum haemorrhage.
2. Some cases of rupture of uterus.
3. Placenta accreta.
4. Couvelaire uterus.
5. Gross uterine infection (postabortive or postpartum).
6. Invasive mole (chorioadenoma destruens).

II. Gynaecological Indications

A. Uterine

1. Congenital. Haematometra which is caused by atresia of the lower genital tract.
2. Traumatic. Injury of uterus during dilatation and curettage or vaginal myomectomy.
3. Inflammatory. Tuberculous endometritis.
4. Neoplastic. Fibroids or malignant diseases of the body or cervix.
5. Miscellaneous. Dysfunctional uterine bleeding, endometriosis, inversion and prolapse.

B. Vaginal

Tumour of the upper two-thirds of the vagina may be treated by radical hysterectomy, pelvic lymphadenectomy, and vaginectomy.

C. Tubal

1. Some cases of bilateral salpingo-oophoritis.
2. Carcinoma of the fallopian tube.

D. Ovarian

1. Malignant ovarian tumour.
2. Benign tumour in a patient above 45 years.

TYPES OF HYSTERECTOMY

1. Abdominal hysterectomy.
2. Laparoscopic abdominal hysterectomy.
3. Vaginal hysterectomy.
4. Laparoscopically assisted vaginal hysterectomy.

Types of Abdominal Hysterectomy

1. Subtotal (supracervical) hysterectomy. The body of the uterus is removed but the cervix is preserved.
2. Total hysterectomy. The body and cervix are removed.
3. Extended hysterectomy. It is total hysterectomy with removal of the medial half of each cardinal ligament, used for treatment of microinvasive cervical carcinoma (stage IA2).
4. Radical hysterectomy. The following structures are removed: the whole uterus, both tubes and ovaries, the broad ligaments, the parametrium, and all the pelvic lymph nodes.
5. Ultraradical hysterectomy. It is pelvic exenteration which may be anterior, posterior, or total pelvic exenteration.
6. Caesarean hysterectomy. Caesarean section is done followed by removal of the uterus as in case of uncontrollable postpartum haemorrhage.

Abdominal hysterectomy may be extrafascial or intrafascial. In extrafascial hysterectomy the uterus is removed with its covering fascial layer and it is the standard operation. In intrafascial hysterectomy the fascia covering the cervix is separated and left attached to the bladder. This allows removal of the cervix without injury of the bladder. It is done when it is difficult to separate the bladder from the cervix as in case of previous caesarean section. It is never done in case of malignancy as lymphatics are present in the fascial layer.

Indications of Radical Hysterectomy

1. Cervical carcinoma, Stage IB or IIA.
2. Endometrial carcinoma, Stage II.
3. Vaginal carcinoma, Stage I or II in the upper two-thirds of the vagina.

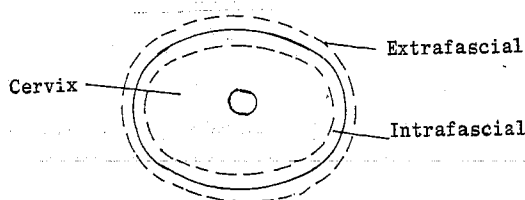


Fig.132. Abdominal hysterectomy

Notes

- Panhysterectomy is an old term indicating total hysterectomy and bilateral salpingo-oophorectomy.
- Before performing hysterectomy, cervical smear should be taken to exclude occult cervical carcinoma.

Disadvantages of Total Hysterectomy

(1) The operation is difficult and takes a longer time; (2) there is more liability to injure the bladder, ureter and rectum; (3) the cervical ligaments are divided with liability to vault prolapse; (4) increased risk of pelvic infection because the vagina is opened; (5) dyspareunia may occur due to shortening of the vagina, presence of a tender scar in its vault and absence of lubricating cervical secretion; (6) absence of cervical (internal) orgasm.

Advantages

(1) It avoids the risk of stump carcinoma; (2) it avoids other complications caused by the retained cervix as chronic discharge; (3) there is a good drainage of the pelvis after the operation because the vagina is opened and so haematoma formation is less common.

Advantages of Subtotal Hysterectomy

(1) Easy and takes a short time; (2) less liability to injure the bladder, ureter and rectum; (3) the cervix is left behind and this protects against vault prolapse; (4) less risk of pelvic infection because the vagina is not opened; (5) it is not followed by dyspareunia.

Disadvantages

(1) Carcinoma may develop in the cervical stump (1-10%); (2) menstruation can occur with a high subtotal hysterectomy; (3) poor drainage of the pelvis after operation because the vagina is not opened and so haematoma formation is more common.

When hysterectomy is performed it should be total to avoid stump carcinoma. However, subtotal hysterectomy is usually done in obstetric cases as postpartum haemorrhage or uterine rupture as the uterus, cervix and vagina form one canal and it is difficult to identify the lower end of the cervix.

VAGINAL HYSTERECTOMY

Indications

It may be indicated in the following conditions:

1. Uterine prolapse.
2. Chronic inversion of uterus.
3. Dysfunctional uterine bleeding.
4. Fibroid uterus and adenomyosis provided that the size of the uterus is not more than 12 weeks pregnancy.

Advantages

1. Safer than abdominal hysterectomy and carries a very low mortality.
2. Shock is rare particularly in obese women.
3. No postoperative discomfort.
4. Short convalescent period.
5. No abdominal scar and incisional hernia.
6. The incidence of intestinal distension, peritonitis, adhesions and intestinal obstruction is rare.
7. An associated prolapse of the vagina can be corrected at the same time.

Disadvantages

1. It is difficult and unsafe in the presence of pelvic adhesions as in case of endometriosis.
2. It does not allow inspection of other abdominal organs.
3. Cannot be done if the size of the uterus is more than 12 weeks pregnancy unless it is bisected during removal.
4. It is not suitable for the treatment of malignant conditions because it does not allow complete removal of all the pelvic lymph nodes and does not allow abdominal exploration.
5. Vault prolapse is more likely than after abdominal hysterectomy.

Note. The ovaries cannot be removed during vaginal hysterectomy in 10-30% of cases.

LAPAROSCOPICALLY ASSISTED VAGINAL HYSTERECTOMY

The laparoscope is used to divide as much of the uterine attachments to free the uterus, which is then removed vaginally. Uterine attachments include infundibulopelvic, round, broad, and cervical ligaments.

Note. Laparoscopic hysterectomy has double the postoperative complications of abdominal hysterectomy.

COMPLICATIONS OF HYSTERECTOMY

I. During Operation

1. Primary haemorrhage.
2. Injury to the bladder, ureter, and intestine.
3. Anaesthetic complications as Mendelson syndrome due to aspiration of vomitus.

II. Postoperative Complications

1. Cardiovascular. Reactionary and secondary haemorrhage, venous thrombosis and pulmonary embolism.
2. Pulmonary. As bronchitis, pneumonia, and lung atelectasis.
3. Gastrointestinal tract. Postoperative distension, vomiting, acute gastric dilatation and paralytic ileus. Peritonitis. Later adhesions and intestinal obstruction.
4. Urinary tract. Urinary tract infection, retention of urine, urinary fistula, ligation of one or both ureters.
5. Complications in the abdominal wound. Infection, burst abdomen, keloid formation and incisional hernia. Incisional hernia is very rare after Pfannenstiel incision (1 in 1250 cases).
6. Genital complications:
 - a. Vaginal discharge due to infection of the vault.
 - b. Vault haematoma.
 - c. Formation of granulation tissue in the vaginal vault. It occurs in about 20% of cases. It leads to vaginal discharge and postcoital bleeding. Treated by cauterization with silver nitrate or electrocautery.
 - d. Vault prolapse.
 - e. Total hysterectomy may be followed by dyspareunia due to shortening of the vagina, presence of a tender scar in the vault, and absence of lubricating cervical secretion.
7. Removal of the ovaries in a young patient will lead to premature menopause with increased risk of osteoporosis. In some cases the ovarian function ceases after hysterectomy due to injury of the ovarian blood supply during the operation. Ovarian failure occurs in about 10% of cases by the end of the 4th year after hysterectomy.
8. Psychological problems resulting from losing the uterus.
9. Mortality rate is about 3 in thousand cases. It is mainly due to haemorrhage, thromboembolism, and septicaemia.

OVARIAN MANAGEMENT AT HYSTERECTOMY FOR BENIGN UTERINE DISEASE

If the uterus is removed for a benign uterine lesion as fibroids or adenomyosis, the ovaries are removed if the patient is postmenopausal or has reached the age of 50 even if she is still menstruating. If the ovaries are healthy and the patient is menstruating and below 50 years, both ovaries or at least one should be preserved to avoid the menopausal syndrome. The risk of cancer arising in the conserved ovary after hysterectomy is rare and occurs in about one per thousand cases. In fact hysterectomy reduces the risk of ovarian cancer by 40%. This may be explained by preventing retrograde menstruation which is said to irritate the ovaries with carcinogens in the menstrual blood. Tubal sterilization has the same effect.

Notes

1. Causes of postoperative vomiting: Effect of anaesthesia, acute gastric dilatation, paralytic ileus, peritonitis, and intestinal obstruction.

2. Causes of postoperative distension. Simple distension may occur on the 2nd postoperative day. Acute gastric dilatation, paralytic ileus, peritonitis, and intestinal obstruction.

TECHNIQUE OF TOTAL ABDOMINAL HYSTERECTOMY

1. The round ligaments are clamped, divided and ligated.
2. The tubes and ovarian ligaments are clamped divided and ligated to conserve the ovaries. If the ovaries have to be removed we clamp, divide and ligate the infundibulopelvic ligaments.
3. The peritoneum of the vesicouterine pouch is incised and extended to open the anterior layer of the broad ligament on both sides.
4. The bladder is dissected downwards.
5. The uterine arteries are clamped, divided, and ligated.
6. The cardinal and uterosacral ligaments are clamped, divided and ligated.
7. The vagina is opened and uterus is removed.
8. The vagina is closed and the stumps of the cardinal, uterosacral, and round ligaments are attached to the vaginal vault to prevent vault prolapse. The vagina may be left open to help drainage of blood from the pelvis.
9. Peritonization of the raw area in the pelvis may or may not be done.

TECHNIQUE OF VAGINAL HYSTERECTOMY

1. Circular incision is made in the vaginal vault around the cervix.
2. The bladder is dissected upwards.
3. The peritoneum of the Douglas pouch and vesicouterine pouch is opened.
4. The cardinal and uterosacral ligaments are clamped, divided and ligated.
5. The uterine arteries are clamped, divided, and ligated.
6. The broad ligaments are clamped, divided, and ligated.
7. The tubes and ovarian ligaments or infundibulopelvic ligaments are clamped, divided, and ligated.
8. The uterus is removed.
9. The pelvic peritoneum is closed or left open followed by closure of vaginal vault.

ENDOMETRIAL ABLATION

Destruction of the endometrium is performed to control dysfunctional menorrhagia when the patient is unfit for hysterectomy as in case of marked obesity, severe hypertension, or diabetes mellitus, and when patient refuses operation. In general endometrial ablation leads to amenorrhoea in 30-60% of patients, hypomenorrhoea in 20-40%, and there is 5-10% failure rate with persistence of menorrhagia. For endometrial ablation, the uterus must be the size of 10 weeks pregnancy or less (length of uterus 12 cm or less).

METHODS

1. Thermal Ablation

Under general anaesthesia the cervix is dilated to 10 mm and an angled probe 10 mm in diameter is inserted into the uterine cavity and slowly rotated 360° over 20 minutes. It destroys the endometrium by heating up to 66° C using electromagnetic energy.

2. Laser Ablation

Under general or local paracervical anaesthesia combined with sedation the endometrium is destroyed by laser through the hysteroscope. YAG or diode laser is used. Laser destroys the endometrium to a depth of 4-5 mm, so the procedure must be done either immediately after menstruation (when endometrium thickness is about 3 mm) or following endometrial suppression with agents such as danazol, progestogens or gonadotrophin releasing hormone analogue. The dose of danazol is 200 mg three times daily for 6 weeks. Also endometrial curettage may be done immediately before the procedure to avoid the use of expensive pre-operative medical therapy.

3. Endometrial Resection

Under general or local paracervical anaesthesia combined with sedation the endometrium is removed (shaved) using the electrocautery cutting loop of the resecting hysteroscope (resectoscope). The loop cuts to a depth of 3-4 mm, so surgery should be done either immediately after menstruation or after endometrial curettage or following endometrial suppression as with laser ablation. Most patients can be discharged from hospital after 3-4 hours. Complications of endometrial resection include uterine perforation, haemorrhage, infection and complications due to absorption of the fluid used to distend the uterus in the form of pulmonary oedema, cerebral oedema, hypertension, dilutional hyponatraemia and dilutional coagulopathy. Also the electric current may be transmitted through the uterine wall leading to burning and damage of the bowel or bladder.

4. Roller Ball Electrocoagulation

A roller ball electrode is fitted to the resectoscope instead of the cutting loop and the endometrium is electrocoagulated. It is easier than resection and carries less risk of perforation. The roller ball is available in diameter ranging from 2 mm and upwards.

5. Thermal Balloon Endometrial Ablation

Performed under general or local paracervical anaesthesia. A latex balloon fixed at the tip of a catheter is inserted into the uterus and then filled with 5% dextrose in water solution (5-30 ml) till the pressure inside the balloon reaches 160-180 mmHg. The fluid is heated to reach a temperature of 87°C which is maintained for 8 minutes. Heat leads to coagulation of the endometrium for a thickness of 3-5 mm. This device is the ThermoChoice System. Another device used is the Cataverm System in which the balloon is filled with 1.5% glycine to

produce a higher pressure of 180-220 mmHg. The fluid is heated to 75°C which is maintained for 15 minutes.

6. Microwave Endometrial Ablation

Microwaves are used to generate a temperature of 70-80°C which is maintained for 2 or 3 minutes. Done under general or local paracervical anaesthesia using a microwave applicator. The endometrium is prepared as mentioned before.

7. Cryo-Ablation

The endometrium is frozen to a temperature of -40°C using carbon dioxide or nitrous oxide. The gas is passed through a probe (Indocryo) to freeze a small amount of normal saline inside the uterus. Saline forms an ice mould to freeze the endometrium. The freezing time is 2 minutes and the depth of endometrial necrosis is 4-5 mm.

8. Hydrothermal Ablation (HTA)

Using the hysteroscope, normal saline at a temperature of 90°C is allowed to circulate around the uterine cavity for 10 minutes at a pressure of 50 mmHg (less than the 70 mmHg opening pressure of the tubal ostia). The depth of necrosis is about 5 mm.

Advantages of Endometrial Ablation over Hysterectomy

1. Can be applied when the patient is unfit for hysterectomy or refuses the operation.
2. Shorter operating time.
3. Shorter stay in hospital.
4. Less postoperative complications.
5. Patient can resume normal activities earlier than those who have undergone hysterectomy.
6. Cost effective.

Disadvantages

1. Not always successful in reducing menstrual loss. Failure rate 5-10%.
2. Dysmenorrhoea may increase.
3. 10-30% of cases will need hysterectomy after 3-4 years due to recurrence of bleeding.
4. The uterine cavity may be obliterated by adhesions and areas of residual endometrium may progress to carcinoma without being recognized.

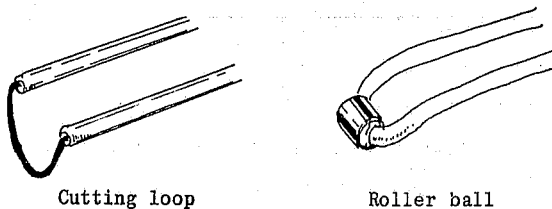


Fig.133. Endometrial ablation

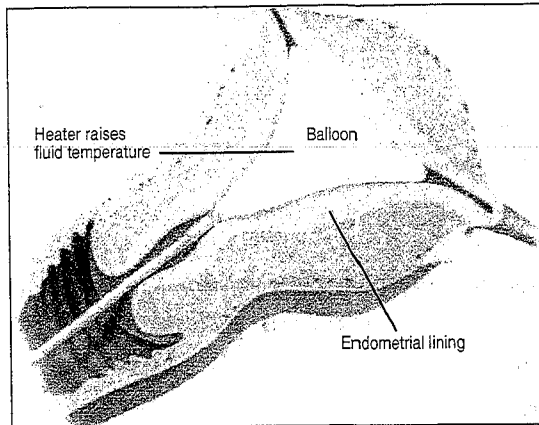


Fig. 133-1. Thermal balloon endometrial ablation

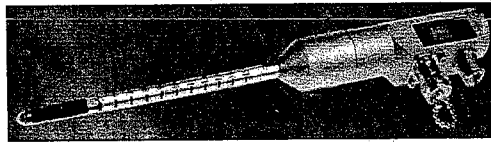


Fig. 133-2. Microwave applicator.

Internal Iliac (Hypogastric) Artery

Indications for Ligation

I. Obstetrical

1. Uncontrollable postpartum haemorrhage due to: (a) uterine atony; (b) placenta accreta; (c) placenta praevia; (d) concealed placental abruption.
2. Broad ligament haematoma.
3. Multiple lacerations of cervix and vagina.

II. Gynaecological

1. Slipping of uterine artery during vaginal hysterectomy.
2. Secondary haemorrhage following vaginal hysterectomy.
3. Radical hysterectomy to reduce bleeding during operation.

Note. Ligation of both hypogastric arteries in case of postpartum haemorrhage stops the bleeding in about 45% of cases, due to the presence of extensive collateral circulation.

RADIOTHERAPY IN GYNAECOLOGY

INDICATIONS

1. Treatment of malignant tumours of the genital tract.
2. Induction of artificial menopause.

MODE OF APPLICATION

1. Brachytherapy (internal radiation). The radio-active source; radium, caesium, or iridium is placed very close to the tumour to be treated, e.g. in the uterus or vagina. It is placed in metal containers (platinum, or tantalum) to screen off alpha and beta rays, and allows only gamma rays. Also the radio-active source may be in the form of needles implanted into the tumour (interstitial radiation).
2. Teletherapy (external radiation). Treatment machines are used in which the source of radiation is distant from the patient. The distance varies from 15 cm to more than one metre, but it is usually one metre. Supervoltage therapy is used.
3. Intraperitoneal instillation of radio-active substances as radioactive colloidal gold or chromic phosphate.

Supervoltage therapy is given by supervoltage machines as cobalt-60, the linear accelerator and the betatron. The supervoltage X-rays pass through the skin with very little absorption and so skin reactions and burns are minimal. This allows unlimited amounts of irradiation to be delivered to the deep tissues in the pelvis without causing harm to the skin. On the contrary the deep X-rays (orthovoltage therapy) are absorbed by the skin and may cause skin injury. For this reason supervoltage (megavoltage) therapy has replaced deep X-rays therapy. Deep X-rays are only used to treat skin cancers.

MODE OF ACTION

1. Direct effect on the cells leading to cell death. Normal cells are more resistant to irradiation than malignant cells. Also the hypoxic cells are less sensitive to irradiation. Placing the patients in hyperbaric oxygen chambers increases the effect of irradiation.
2. Indirect effect on the cells by causing fibrosis and obliteration of the blood vessels in the tumour bed thus leading to ischaemia and death of the tumour cells.
3. Systemic effect or radiation sickness. This is characterized by nausea, vomiting, loss of appetite, loss of weight, malaise and pyrexia. This is due to liberation of histamine-like substances from the necrotic tissues.

INSERTION OF THE RADIOACTIVE MATERIAL

It is performed under general anaesthesia. Bladder is evacuated and cervix dilated. The empty containers are placed first in the uterus and then in the lateral vaginal fornices. The vagina is packed with gauze soaked in flavine to prevent displacement of the containers. A plain X-ray is taken to be sure that the containers are in the proper place. Radium, caesium, or

iridium is then loaded in the applicators. This afterloading technique ensures accurate placement of the applicators and save the medical staff from excessive exposure to radiation. The patient is kept in bed with a catheter fixed in the bladder and given a low-residue diet until the applicators are removed.

COMPLICATIONS OF RADIOTHERAPY

1. Radiation sickness. Treated by antihistaminics and antiemetics.
2. Skin reaction and burns occur with deep x-rays but very rare with supervoltage therapy.
3. Flaring up of pelvic infection leading to pyometra, parametritis, septicaemia and peritonitis. This is the main cause of the primary mortality which occurs in less than 1% of cases.
4. Injury of the urinary tract in the form of cystitis, ulceration of the bladder and fistula. Ureteric obstruction may occur from fibrosis of the parametrium causing hydronephrosis and finally uraemia. The vesicovaginal fistula results from ischaemic necrosis and usually occurs 3-9 months after irradiation or even later. This fistula is usually treated by urinary diversion. However, it can be treated by colpocleisis or closure using a flap from the rectus or gracilis muscle or bulbocavernosus muscle and fat. The latter is known as Martius graft.
5. Injury of the gastrointestinal tract in the form of proctitis, sigmoiditis and enteritis, small bowel stricture and obstruction, ulceration, rectovaginal fistula and rectal stenosis. This rectovaginal fistula is managed by colostomy.
6. Depression of the bone marrow with anemia and leucopenia.
7. Bone necrosis and fracture of the femur neck.
8. Chronic pelvic pain or pain along the sciatic nerve due to neuritis or fibrosis.
9. Cervical stenosis with pyometra, vaginal stenosis and dyspareunia.
10. Radiation menopause. This can lead to severe menopausal symptoms which are treated by hormone replacement therapy.

RADIOTHERAPY FOR CERVICAL CARCINOMA

Radium, caesium, or iridium is inserted into the uterus and lateral vaginal fornices. This is preceded or followed by supervoltage therapy directed to the pelvis, to radiate the tumour itself, the parametria, and pelvic lymph nodes. The aim is to deliver 7000-8000 r or cGY to the tumour and 5000 r (cGY) to the parametria and lymph nodes. The dose must not exceed 4000 r (cGY) to the rectum and 5000 r (cGY) to the bladder. There are 3 leading schools for the application of radium. They are known by the city of origin.

Note. r is the rad unit. GY is the new Gray unit and equals 100 rads. cGY is centigray and equals one rad. So 7000 r=7000 cGY=70 GY.

1. The Paris Technique

A small dose of radium (66.6 mg) is applied in the uterus and lateral vaginal fornices and left for 120 hours (5 days). This is followed by external irradiation to the pelvis.

2. The Stockholm Technique

The dose of radium varies from one patient to the other, the average dose is 110 mg. of radium applied for 24 hours. After 3 weeks, radium is applied again. This is followed by external irradiation to the pelvis.

3. The Manchester Technique

Radium is applied in the uterus and lateral vaginal fornices. It is calculated to deliver 7000-8000 r to point A and 3000 r at point B. Radium is applied on two sittings, each lasting 3 days (72 hours) with an interval of 3 days in between. Point A is situated 2 cm lateral to the centre of the cervix and 2 cm above the vaginal vault and corresponds to the paracervical lymph node found at the crossing of the ureter and uterine artery. Point B is 3 cm lateral to point A and corresponds to the obturator lymph nodes.

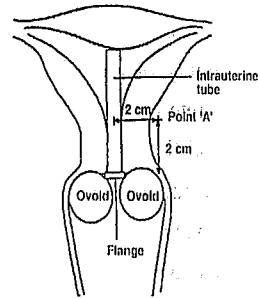


Fig. 133-3. The Manchester system for treatment of cancer of the cervix; Point "A".

The contraindications of radiotherapy in cervical carcinoma and its advantages and disadvantages have been mentioned with treatment of cancer of cervix.

RADIOTHERAPY FOR ENDOMETRIAL CARCINOMA

The results of radiotherapy alone are inferior to surgery. It is given if the patient is not fit for surgery or the growth is too advanced for surgery. Radiotherapy can be given using the Stockholm method (Heyman packing technique). The uterine cavity is packed with 10-20 Heyman capsules each containing 8 mg radium. The uterus is packed until it can no more accommodate any capsules (packing technique). At the same time a special applicator containing 100-150 mg radium is placed in the vaginal vault. Two treatments are given, each for 20 hours, and separated by an interval of one week. This is followed by external pelvic radiation to deliver 4000-5000 rads (40-50 GY).

Note. Caesium has now replaced radium because caesium is cheaper, readily available as it is produced artificially and has a shorter life span so more safer for the medical staff handling it.

GYNAECOLOGICAL INSTRUMENTS

CUSCO VAGINAL SPECULUM

It is a self-retaining speculum. It is of different sizes: small, medium and large.

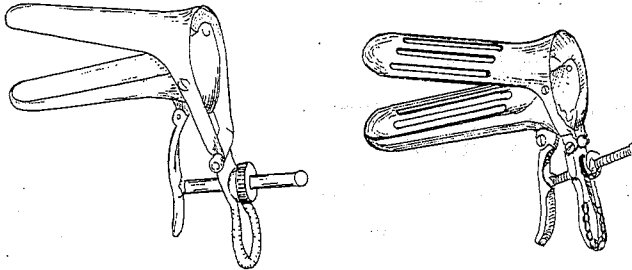


Fig.134. Cusco vaginal speculum

Mode of Application

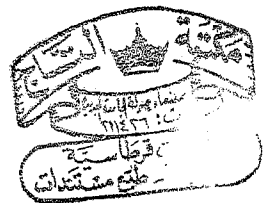
The labia are separated with the index and thumb of the left hand. The lubricated closed speculum is introduced into the vagina edgewise. As it is pushed inside, it is rotated at right angle so that the blades become anterior and posterior. The blades are then opened to expose the cervix and vaginal walls. The blades can be kept separated by using the screw.

Types

1. Non-fenestrated type. It does not allow inspection of the anterior and posterior vaginal walls. However, the walls are inspected while the speculum is withdrawn gradually.
2. Fenestrated type. It allows partial inspection of the anterior and posterior vaginal walls. However, it does not protect the vaginal walls during cauterization of the cervix.

Indications

1. To examine the cervix and vaginal walls.
2. To take cervical smear to examine for malignant cells.
3. To take cervical and high vaginal swab to examine for micro-organisms.
4. To allow introduction of uterine sound.
5. To allow insertion of intrauterine contraceptive device.
6. To carry out hysterosalpingography.
7. To apply treatment to the cervix as cauterization.
8. To do postcoital test.
9. To carry out artificial insemination.



FERGUSON SPECULUM

It is of different sizes. It was used in the past to protect the vaginal walls during chemical cauterization of the cervix with silver nitrate solution to treat cervical erosion. The end is bevelled because the posterior vaginal wall is longer than the anterior wall.

SIMS SPECULUM

One blade is bigger than the other to fit the size of the vagina. It is mainly used to inspect the anterior vaginal wall in case of vesicovaginal fistula. The patient should be in Sims or left lateral position. Also genital prolapse is best examined by Sims speculum with the patient in the left lateral position. See page 87.

AUVARD VAGINAL SPECULUM

It is a self-retaining posterior vaginal speculum. It is applied with the patient under general anaesthesia because of its heavy weight. It is used during vaginal operations as evacuation. The grooved shaft allows drainage of blood. The wings may have small holes to fix the speculum to the towels covering the patient using towel clips or silk stitches.

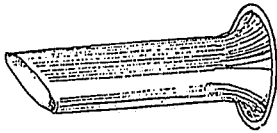


Fig.135. Fergusson speculum

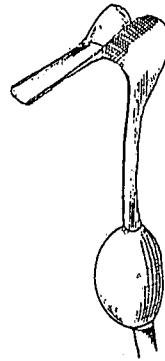


Fig.136. Auvard vaginal speculum

DOYEN VAGINAL RETRACTOR

It is used during vaginal operations to retract the vaginal wall.

VULVAL RETRACTOR

It was used in the past during vaginal operations to expose the lower vagina and urethra. Now, this exposure is carried out by stitching the labia minora to the surrounding towels covering the patient.

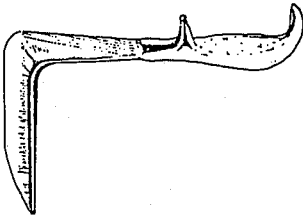


Fig.137. Doyen vaginal retractor

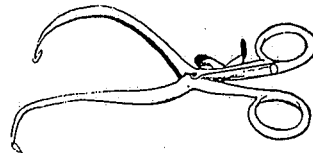
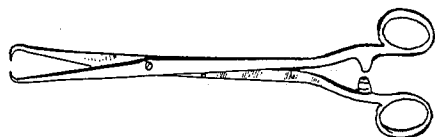
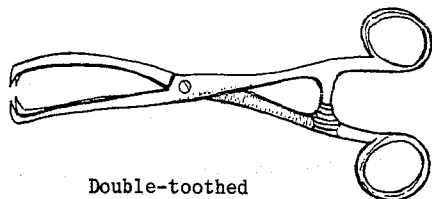
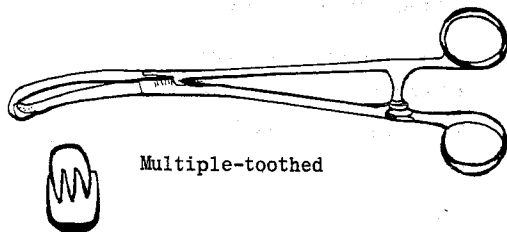


Fig.138. Vulval retractor

VULSELLUM (VOLSELLUM) FORCEPS**Indications**

1. To grasp the cervix in absence of pregnancy.
2. To grasp a fibroid polyp during vaginal myomectomy.
3. To rupture the bag of forewaters to induce labour. However, this is done by the Amnihook.

The vulsellum may be single-toothed, double-toothed or multiple-toothed. The single-toothed vulsellum causes less damage to the cervix when it slips but the grasp is weak and so more liable to slip. The multiple-toothed vulsellum has a good grasp but more traumatic to the cervix when it slips.

**Single-toothed****Double-toothed****Multiple-toothed****Fig.139. Vulsellum****UTERINE SOUND**

See page 376.

CERVICAL DILATORS

See page 378.

UTERINE CURETTES

See page 381.

VABRA ASPIRATOR

See page 266.

AYRE WOODEN SPATULA

See page 233.

CERVICAL BIOPSY FORCEPS

To take cervical biopsy to exclude malignancy.

CANNULA FOR HYSTEROSALPINGOGRAPHY

See page 383.

URINARY CATHETERS

See page 377.

THE HYSTEROSCOPE

See page 386.

THE LAPAROSCOPE

See page 391.

CORKSCREW MYOMA EXTRACTOR (DOYEN)

It may be used to pull out the myoma during myomectomy.

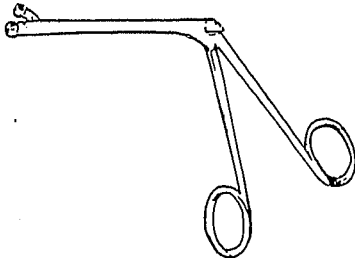


Fig.140. Cervical biopsy forceps

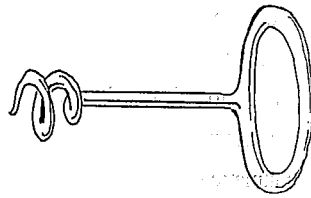


Fig.141. Corkscrew myoma extractor

BONNEY MYOMECTOMY CLAMP

It is applied on both sides of the lower part of the uterus just above the cervix to compress the uterine arteries to minimize blood loss during abdominal myomectomy. The blades should be covered with a rubber tube to avoid crushing of the uterine wall. Instead a rubber catheter is preferred because it is less traumatic and both uterine and ovarian arteries are occluded. (See page 395).

UTERINE HOLDING FORCEPS

It is used to pull the uterus upward during abdominal hysterectomy and other abdominal gynaecological operations.

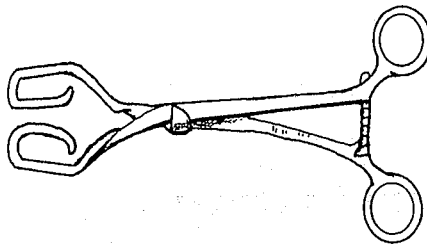


Fig.142. Uterine holding forceps

WERTHEIM CLAMP

It is used during Wertheim operation to close the vagina to prevent implantation of malignant cells into the vagina, vulva, pelvic cavity, or abdominal wall.

OVARIAN TROCAR AND CANNULA

It is used to evacuate the contents of a large ovarian cyst to be able to remove it through a small abdominal incision.

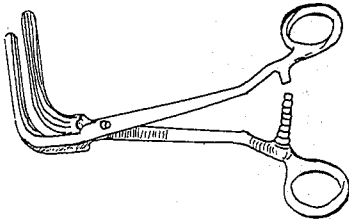


Fig.143. Wertheim clamp



Fig.144. Ovarian trocar and cannula

KEGEL PERINEOMETER

It is used for pelvic floor exercises after delivery to protect against genital prolapse and for treatment of stress incontinence. (See page 337).

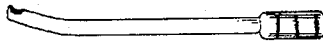


Fig. 145. Suction curette for suction evacuation

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